静岡医療センター研究業績集（24）

(2016 年度)

静岡医療センター臨床研究部

発刊の辞

2016年の静岡医療センター臨床研究部業績集が完成いたしました。田邊臨床研究部長ならびに臨床研究部の職員のかたがたの努力に感謝いたします。

学会発表数はほぼ横ばいですが、論文数、特に英文論文数が大幅に増加しています。診療で多忙な中で多くの職員が臨床研究に成果を上げてくれていることに改めて感謝いたします。

静岡医療センターは平成２９年１０月に同じ国立病院機構の静岡富士病院の機能を統合して再出発する予定です。これまで急性期医療のみでしたが、今後は重症心身障害と神経難病に対する医療にも取り組みます。それに伴い臨床研究部にも神経難病に関する部門が設置される予定です。研究の幅がさらに広がるものと期待しています。

２０２５年に向けて地域医療の再検討が行われ、医療と介護、在宅医療との連携の確率が急務となっています。また迷走しながらも新専門医制度も始まろうとしています。枠組みや制度が変わっても医療の本質や臨床研究の重要性に変わりはないものと信じています。今後も静岡医療センター臨床研究部の活動をご支援くださるようお願い申しあげます。

2017年9月

独立行政法人国立病院機構静岡医療センター
院長　梅本琢也

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はじめに

国立病院機構の使命として質の高い臨床研究と治験の推進を掲げています。静岡医療センターもその基本指針に健康科学の推進を挙げており、当臨床研究部がその責務を担っています。
平成28年度の臨床研究部活動をまとめましたのでご報告いたします。

１．臨床研究部の概要

（１）設置年度

設置年度：平成３年１０月

（２）組　　織

５研究室および治験管理室

	氏　　名	専任・併任の別	備　　考
臨床研究部長	田邊　潤	専任	治験管理室長併任
循環動態研究室長	小鹿野道雄	併任	循環器内科部長
病因病態研究室長	志田幹雄	併任	内科部長
治療開発研究室長	黒田勝宏	併任	脳神経外科部長
人工臓器研究室長	高木寿人	併任	心臓血管外科部長
医療情報処理研究室長	杉山　彰	併任	放射線科診療部長

２．施設の機能付与及び特徴

臨床機能上は循環器・がん・救急・総合診療を4本柱として、静岡県東部の急性期基幹医療施設として診療に当たっています。独立行政法人国立病院機構の東海北陸地方における循環器病の基幹施設に指定され、静岡県地域がん診療連携推進病院に指定されています。
また、地域医療支援病院としての役割を担っています。

３．これまでの臨床研究部の主な活動状況

臨床研究部は主として循環器病およびその関連疾患に関する病因、病態、診断、治療、予防対策、社会復帰を含む予後調査等についての系統的研究を行なってきましたが、独立行政法人化に伴う病院機能の見直しとともに、循環器に限定せず、がん・総合診療を始め看護部門等での臨床研究にも幅広く支援を行っています。
これまでの主な研究テーマは循環器系では（１）動脈硬化性疾患の危険因子への対策に関する研究（２）虚血性心疾患、脳卒中、大動脈瘤、末梢血管疾患の病態及び先進的治療に関する研究（３）循環器病の予後調査に関する研究です。がんでは消化器内科、外科を中心に肝胆膵での業績が多くあげられています。
臨床研究部での研究は、これらの臨床活動により得られた資料を有効に活用しながら診療の水準を向上させることを目的としています。

４．平成28年度活動の概要

本年度は昨年度と比べて学会発表、論文発表ともに増加しております。欧文での論文発表数が一昨年に比べると減少しているため、さらなる努力が必要であると考えられます。
平成27年4月に『人を対象とする医学系研究に関する倫理指針』が施行され、指針に則って臨床研究審査委員会で臨床研究の倫理審査をおこなっています。

５．平成28年度に獲得した研究費

（1）国立病院機構共同臨床研究

課題名	研究者	研究費
エビデンスに基づいた重症糖尿病足壊疽の治療法の策定に関する国際（日独）共同研究	梅本琢也（心臓血管外科）	3.5 万円
看護学生の心理的バイタルサイン（Psychological vital sing:PVS）の標準化と自己診断システムの構築に関する研究	三浦美和子（看護師）	8.6 万円
多施設共同抗がん薬曝露実態調査と医療従事者の安全確保のための「Hazardous Drugs の安全な取り扱い」の概念構築	梅本琢也（心臓血管外科）	5.0 万円

６．受託研究に関する実績

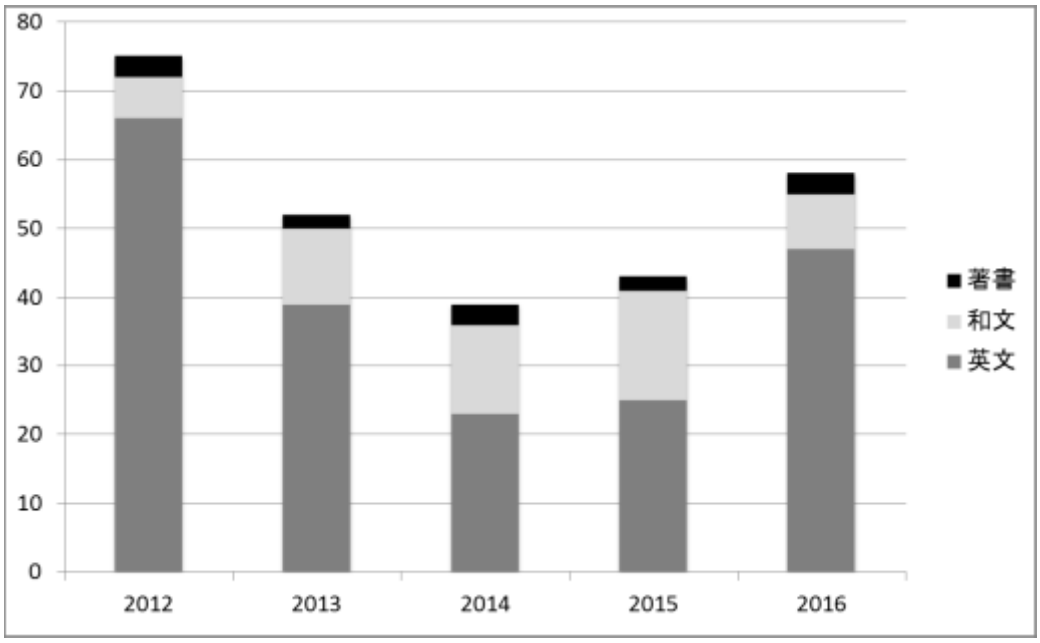
件　数	受託金額	実施率	治験審査委員会登録の有無
31件	31635 千円	61.9%	有

７．平成28年度の研究発表

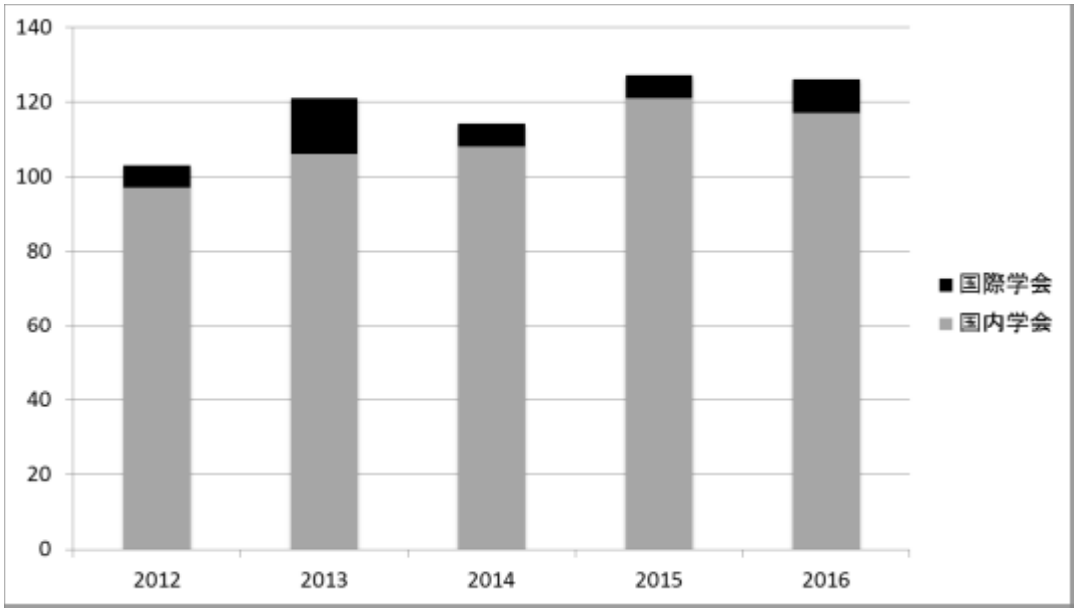
（１）学会発表：国内　118件、国際　8件、　　合計　126件
（２）論文発表：邦文　　8編、欧文 47編、　　合計　55編

※ ただし、学会抄録、研究班報告書は含まない。
※ 欧文はLetterも含む

論文発表数の推移



学会発表数の推移



８．受託研究審査委員会

委員長　：　田邊　潤　　（臨床研究部長）
副委員長：　中野　浩　　（副院長）
外部委員：　杉村　伸一　　（社会福祉法人静岡恵明学園赤ちゃんセンター静岡恵明学園園長）
　　青木　千賀子　（日本大学国際関係学部教授）
　　亀　　廣之　　（臥雲寺住職）
委　員　：　小澤　章子　　（統括診療部長）
委　員　：　河合　憲一　　（医局長）
委　員　：　川中　秀和　　（副医局長）
委　員　：　古山　雅博　　（事務部長）
委　員　：　小林　智晴　　（薬剤部長）
委　員　：　眞田　正世　　（看護部長）
委　員　：　成田　博　　（企画課長）
委　員　：　北山　淳一　　（業務班長）

９．2016年度新規受託研究一覧

（１）治験

研究課題	依頼者	責任医師
ハイリスクの非転移性去勢抵抗性前立腺癌を有する男性を対象としたODM-201の有効性及び安全性を検討する多国間、無作為化、二重盲検、プラセボ対照、第Ⅲ相臨床試験	バイエル薬品株式会社	泌尿器科 部長 間庭章光
駆出率低下を伴う日本人心不全患者を対象としたomecamtiv mecarbilの安全性、薬物動態、及び有効性を評価する無作為化二重盲検プラセボ対照多施設共同試験	アステラス・アムジェン・バイオファーマ株式会社	循環器内科 臨床研究部長 田邊　潤

（２）製造販売後臨床試験・使用成績調査

研究課題	依頼者	責任医師
オルドレブ点滴静注用150mg使用成績調査	グラクソ・スミスクライン株式会社	外科 中野良太
ヴィキラックス配合錠　使用成績調査	アッヴィ合同会社	消化器内科 部長 大西佳文
アノーロエリプタ30吸入用使用成績調査	グラクソ・スミスクライン株式会社	呼吸器内科 本橋典久
インフリキシマブ BS 点滴静注用 100mg「NK」-クローン病および潰瘍性大腸炎を対象とした長期の特定使用成績調査	日本化薬株式会社	消化器内科 部長 大西佳文
ヨンデリス点滴静注用0.25 mg / 1 mg 特定使用成績調査（全例調査）	大鵬薬品工業株式会社	消化器内科 部長 大西佳文
リクラスト点滴静注液 5 ㎎特定使用成績調査(長期使用に関する調査)	旭化成ファーマ株式会社	整形外科 部長 太田周介
レパーサ皮下注140mg 特定使用成績調査（長期使用）	アステラス・アムジェン・バイオファーマ株式会社	循環器内科 臨床研究部長 田邊　潤
レミケード点滴静注用 100（川崎病の小児に関する調査） 特定使用成績調査	田辺三菱製薬株式会社	小児科 医長 渡邉　誠

（３）副作用詳細調査

研究課題	依頼者	責任医師
アクテムラ副作用詳細報告	中外製薬株式会社	整形外科 部長 太田周介

アドソルビン原末副作用詳細調査	第一三共株式会社	外科 医長 宮原利行
エナラプリルマレイン酸塩錠 2.5m g 「サワイ」副作用詳細報告	沢井製薬株式会社	循環器内科 医長 川中秀和
エナラプリルマレイン酸塩錠 2.5m g 「サワイ」副作用詳細報告	沢井製薬株式会社	循環器内科 鈴木啓士
エリキュース錠有害事象詳細調査	ブリストル・マイヤーズ スクイブ株式会社	脳神経外科 高橋照男
オイパロミン注で発現した重篤な副作用 （アナフィラキシーショック）の詳細調査	コニカミノルタ株式会社	放射線科 診断部長 阿部彰子
サムスカ錠副作用･感染症報告	大塚製薬株式会社	心臓血管外科 医長 河合憲一
サムスカ錠副作用･感染症報告	大塚製薬株式会社	心臓血管外科 三ツ田翔平
チエナム点滴静注用副作用詳細報告	MSD 株式会社	外科 加藤喜彦
フィニバックス点滴静注用 0.25ｇの 副作用調査	塩野義製薬株式会社	心臓血管外科 三ツ田翔平
ボンビバ静注副作用詳細報告	中外製薬株式会社	整形外科 土井孝信
メスチノン錠 60mg による副作用詳細調査	共和薬品工業株式会社	循環器内科 医長 田尻正治
メルカゾール錠 5mg　副作用詳細報告	あすか製薬株式会社	循環器内科 部長 小鹿野道雄
ラニラピッド副作用詳細報告	中外製薬株式会社	心臓血管外科 医長 河合憲一
ランソプラゾール OD 錠 15m ｇ「サワイ」 副作用詳細報告	沢井製薬株式会社	消化器内科 伊藤弘昭

（４）医療機器

研究課題	依頼者	責任医師
アルチマスター使用成績調査（使用実態調査）	テルモ株式会社	循環器内科 臨床研究部長 田邊　潤

切除不能悪性胆管狭窄に対するゼオステントの有用性調査	ゼオンメディカル株式会社	消化器内科 部長 大西佳文
人工股関節セラミック骨頭「BIOCERAM AZUL ヘッド」の市販後使用成績調査	京セラメディカル株式会社	整形外科 部長 太田周介
血管用ステント「イノーバ バスキュラーステント」の使用調査および SFA 市場実態調査	ボストン・サイエンティフィックジャパン株式会社	循環器内科 臨床研究部長 田邊　潤
吸収性体内固定用ピン「グランドフィックス」の臨床使用実態調査	グンゼ株式会社	心臓血管外科 部長 高木寿人
フックピンテンションバンドワイヤリングシステム製造販売後調査	メディカルトラスト株式会社	整形外科 部長 太田周介

10. 臨床研究審査委員会

委員長　：　田邊　潤　　（臨床研究部長）
副委員長：　中野　浩　　（副院長）
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委　員　：　眞田　正世　　（看護部長）
委　員　：　成田　博　　（企画課長）
委　員　：　北山　淳一　　（業務班長）

（１）当院のみ実施

研究課題	研究責任者
兎眼症例の結膜杯細胞数とレバミピド点眼液の効果の検討	眼科 部長 出口雄三
不眠症プロトコルに基づく薬物治療管理の導入とその評価	薬剤部 調剤主任 薄　雅人
エルデカルシトール投与後の腎機能悪化に関連する因子の検討	薬剤部 薬務主任 内野達宏
皮膚乾燥のある高齢女性患者への１日２回の保湿剤塗布援助の有効性	看護師 辻村美樹

（２）多施設共同研究

研究課題	研究代表機関	研究責任者
高齢心不全患者の心不全の急性増悪による再入院に関する因子の検討	独立行政法人国立病院機構 静岡医療センター	リハビリテーション科 鬼頭和也
関節リウマチ患者におけるリンパ増殖性疾患に関する研究	東京女子医科大学 膠原病リウマチ痛風センター	整形外科 部長 太田周介
薬物代謝酵素誘導能を有する薬剤が脂質異常症の発症に及ぼす影響	独立行政法人国立病院機構 静岡てんかん・ 神経医療センター	薬剤部 製剤主任 彦坂麻美
大腿骨頭すべり症に関する多施設共同前向き観察研究（レジストリ研究）	地方独立行政法人 大阪市民病院機構 大阪市立総合医療センター	整形外科 部長 太田周介

（３）委託研究

研究課題	研究依頼者	研究責任者
フックピンテンションバンドワイヤリングシステム製造販売後調査	メディカルトラスト 株式会社	整形外科 部長 太田周介
吸収性体内固定用ピン「グランドフィックス」の臨床使用実態調査	グンゼ株式会社	心臓血管外科 部長 高木寿人
血管用ステント「イノーバ バスキュラーステント」の使用調査および SFA 市場実態調査	ボストン・サイエンティフィックジャパン 株式会社	循環器内科 臨床研究部長 田邊　潤
人工股関節セラミック骨頭「BIOCERAM AZUL ヘッド」の市販後使用成績調査	京セラメディカル 株式会社	整形外科 部長 太田周介
切除不能悪性胆管狭窄に対するゼオステントの有用性調査	ゼオンメディカル 株式会社	消化器内科 部長 大西佳文
アルチマスター使用成績調査 （使用実態調査）	テルモ株式会社	循環器内科 臨床研究部長 田邊　潤

発表論文・著書・学会発表・講演

2016 年度論文発表

【消化器内科】

１）八橋　弘、大西佳文、梅村　俊、須賀哲也、上崎利昭、山下純子、
井廻道夫
肝硬変患者における血漿アルブミンのレドックス状態の変化と分岐鎖アミノ酸配合顆粒投与の影響
新薬と臨床 2016;65(7)916-932

２）大西佳文、伊藤弘昭、近藤　高、榎澤哲司、加藤喜彦、宮原利行、
角　泰廣、中野　浩、清水敦夫、杉山　彰、齋藤光次、近藤福雄
悪性転化が疑われた肝内門脈肝静脈短絡症併存の炎症性肝細胞腺腫の 1 症例
Liver Cancer. 2016(22)47-51

【循環器内科】

１）Michio Ogano, Yu-ki Iwasaki, Jun Tanabe, Hisato Takagi, Takuya Umemoto, Meiso Hayashi, Yasusi Miyauchi, Wataru Shimizu.
Restoration of ventricular septal hypoperfusion by cardiac resynchronization therapy in patients with permanent right ventricular pacing.
Int J Cardiol. 2016(224)353-359.

【整形外科】

１）Bito S, Miyata S, Migita K, Nakamura M, Shinohara K, Sato T, Tonai T, Shimizu M, Shibata Y, Kishi K, Kubota C, Nakahara S, Mori T, Ikeda K, Ota S, Minamizaki T, Yamada S, Shiota N, Kamei M, Motokawa S.
Mechanical prophylaxis is a heparin-independent risk for anti-platelet factor 4/heparin antibody formation after orthopedic surgery.
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２）澤味小百合
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発表論文集

原著ならびに症例報告の原文抄録を掲載しました。

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原　著

肝硬変患者における血漿アルブミンのレドックス状態の変化と分岐鎖アミノ酸配合顆粒投与の影響

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要　旨

肝硬変患者は，低アルブミン血症になっていることが知られているが，本研究ではアルブミンのレドックス（酸化/還元バランス）状態の評価を行った。その結果，肝硬変患者では，腹水なし，軽度，中等度の順でアルブミン濃度が有意に低くなっていたが，還元型アルブミンの比率も同様に有意に低率であり，酸化ストレスを受けている患者が多いと考えられた。浮腫に関しても同様の結果であった。

一方，分岐鎖アミノ酸配合顆粒は，肝硬変患者の低アルブミン血症を改善すること（アルブミン濃度の上昇）が知られているが，投与開始時の還元型アルブミン比が低下（65%以下）している患者においては，分岐鎖アミノ酸投与により還元型アルブミンの比率が有意に高くなり，酸化ストレスを軽減していると考えられた。また，分岐鎖アミノ酸は肝硬変患者の腹水，浮腫および自覚症状（全身倦怠感，易疲労感，こむら返り等）を改善した。還元型アルブミン比が低下しており，なおかつ分岐鎖アミノ酸投与後にアルブミン濃度が上昇しなかった患者においても，腹水，浮腫および自覚症状が改善・非発現の症例では還元型アルブミン比率が有意に上昇していた。症状不変・悪化群ではそのような有意な変化は認められなかった。

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症例報告
Case Report

悪性転化が疑われた肝内門脈肝静脈短絡症併存の炎症性肝細胞腺腫の1症例

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A case of doubtful malignant transformed inflammatory hepatocellular adenoma with portal-hepatic venous shunt

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抄録：肝S4S5に中心部を除き造影早期相で強い造影効果と後期相で弱い造影効果を有する辺縁分葉状の8 cm大腫瘍は，生検で炎症性肝細胞腺腫(inflammatory hepatocellular adenoma : I-HCA)と診断された。6か月後，9 cm大に増大し，EOB-MRI肝細胞相で内部は弱い低信号域で，辺縁のみEOBを取り込む腫瘍で，悪性転化の可能性も否定できず再生検した。免疫組織も含め総合診断しHCCへの悪性転化を考えたが，肝内門脈肝静脈短絡症(portal-hepatic venous shunt : PVシャント)による肝機能低下のため手術は断念し，厳重に経過観察している症例である。

Key words：炎症性肝細胞腺腫，肝内門脈肝静脈短絡症，悪性転化，肝細胞癌

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はじめに

肝細胞腺腫(HCA)は，欧米では若い女性に多く経口避妊薬との関与が指摘される比較的稀な疾患であるが，日本では，男性例が多く，経口避妊薬との関与も少ないとされている。また，悪性転化については，欧米で5～10％の報告[1-3]もあるが，本邦における明確な報告はなくcontrovercialな問題である。自験例は，WHO分類[4]のI-HCA(inflammatory hepatocellular adenoma)に相当するが，成因としてPVシャントの関与が推察され，さらに経過観察中に増大し悪性転化も疑われた症例であり，興味深いと考えられたので報告する。

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Restoration of ventricular septal hypoperfusion by cardiac resynchronization therapy in patients with permanent right ventricular pacing☆

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ABSTRACT

Background: Pacing from the right ventricular apex (RVA) is associated with cardiac dysfunction and shows electrophysiological features similar to left bundle branch block in which left ventricular (LV) mechanical dyssynchrony impairs septal coronary artery perfusion.

Methods: A total of 62 non-ischemic patients with an implanted pacemaker at the RVA with a pacing rate of >95% were studied. LV septal coronary perfusion as indicated by the LV septal perfusion index was measured by electrocardiography (ECG)-gated single-photon emission computed tomography for all patients at baseline and for patients who were upgraded to CRT at 6 months after CRT. Relationships among LV septal perfusion index, QRS duration, and LV ejection fraction were analyzed.

Results: Among the patients with permanent RVA pacing, 28 of 62 (45%) had impaired septal perfusion (i.e., septal perfusion index <0.9). The LV septal perfusion index was significantly correlated with both QRS duration ($r = -0.763$, $p < 0.001$) and LV ejection fraction ($r = 0.462$, $p = 0.001$). Eleven patients were upgraded to CRT. CRT significantly improved the LV septal perfusion index from 0.63 (SD = 0.13) to 0.89 (SD = 0.19) ($p < 0.001$)and cardiac function: LV end-systolic volume from 102.3 mL (SD = 70.0) to 179.7 mL (SD = 118.4) ($p = 0.002$) and LV ejection fraction from 22.5 (SD = 8.9%) to 38.4% (SD = 13.9%) ($p = 0.001$).

Conclusions: Nearly half of the non-ischemic patients with permanent RVA pacing presenting with prolonged QRS duration and LV dysfunction developed LV septal hypoperfusion. Both septal perfusion and LV function improved in patients who were upgraded to CRT.

1. Introduction

The right ventricular apex (RVA) is a standard pacing site for ventricular lead placement. However, some patients with permanent RVA pacing experience deleterious effects on left ventricular (LV) systolic function and have high re-hospitalization rates [1–5]. Several studies evaluating LV function by echocardiography noted that mechanical ventricular dyssynchrony induced by RVA pacing played a role in reducing LV function [6–8]. In those patients with worsening LV function due to RVA pacing, upgrading to cardiac resynchronization therapy (CRT) reestablished LV synchrony, improving LV function and clinical outcomes [9–13].

In a recent study, LV dyssynchrony induced by RVA pacing was associated with reduced coronary blood flow evaluated using transthoracic echocardiography to measure the velocity time integral of the distal portion of the left anterior ascending artery (LAD) [14]. Furthermore, CRT was found to increase LAD velocity time integral in these patients [15]. However, the use of transthoracic echocardiography to evaluate coronary perfusion is limited by a restricted echo-window area and inter-observer error.

The objectives of this study were to assess coronary artery perfusion using single-photon emission computed tomography (SPECT) and to evaluate the clinical effect of CRT in patients with permanent RVA pacing.

☆ Ogano M, Iwasaki Y, and Tanabe J take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. Takagi H assisted with device implantation and followed up patients. Umemoto T supervised operation of device implantation. Hayashi M and Miyauchi Y assisted with interpretation of preliminary data. Shimizu W supervised this study and critically reviewed the manuscript.

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Regular Article

THROMBOSIS AND HEMOSTASIS

Mechanical prophylaxis is a heparin-independent risk for anti–platelet factor 4/heparin antibody formation after orthopedic surgery

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Key Points

- Patients undergoing total knee arthroplasty can develop anti-PF4/heparin antibodies without heparin exposure.
- Dynamic mechanical prophylaxis is a heparin-independent risk factor for anti-PF4/heparin antibody formation in this patient population.

Platelet-activating antibodies, which recognize platelet factor 4 (PF4)/heparin complexes, induce spontaneous heparin-induced thrombocytopenia (HIT) syndrome or fondaparinux-associated HIT without exposure to unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). This condition mostly occurs after major orthopedic surgery, implying that surgery itself could trigger this immune response, although the mechanism is unclear. To investigate how surgery may do so, we performed a multicenter, prospective study of 2069 patients who underwent total knee arthroplasty (TKA) or hip arthroplasty. Approximately half of the patients received postoperative thromboprophylaxis with UFH, LMWH, or fondaparinux. The other half received only mechanical thromboprophylaxis, including dynamic (intermittent plantar or pneumatic compression device), static (graduated compression stockings [GCSs]), or both. We measured anti-PF4/heparin immunoglobulins G, A, and M before and 10 days after surgery using an immunoassay. Multivariate analysis revealed that dynamic mechanical thromboprophylaxis (DMT) was an independent risk factor for seroconversion (odds ratio [OR], 2.01; 95% confidence interval [CI], 1.34-3.02; $P = .001$), which was confirmed with propensity-score matching (OR, 1.99; 95% CI, 1.17-3.37; $P = .018$). For TKA, the seroconversion rates in patients treated with DMT but no anticoagulation and in patients treated with UFH or LMWH without DMT were similar, but significantly higher than in patients treated with only GCSs. The proportion of patients with ≥1.4 optical density units appeared to be higher among those treated with any anticoagulant plus DMT than among those not treated with DMT. Our study suggests that DMT increases risk of an anti-PF4/heparin immune response, even without heparin exposure. This trial was registered to www.umin.ac.jp/ctr as #UMIN000001366. (*Blood*. 2016;127(8):1036-1043)

Introduction

Heparin-induced thrombocytopenia (HIT) is caused by platelet-activating antibodies (HIT antibodies), mostly against platelet factor 4 (PF4)/heparin complexes.[1] When heparin makes a complex with PF4 in an optimal stoichiometric ratio, heparin induces conformational changes in PF4, thereby exposing neoantigens that trigger immune responses, which in turn generate anti-PF4/heparin antibodies.[2,3] Thus, the frequency of anti-PF4/heparin antibody formation depends on pharmacologic factors such as the type,[4] exposure duration,[5] and plasma concentration[2,3] of heparin. However, recent studies have also demonstrated that nonpharmacologic factors, such as the type of surgery[3] and extent of trauma,[6] also influence risk of anti-PF4/heparin immunization. An additional issue is that certain nonheparin polyanions, such as bacterial surfaces, nucleic acids, and hypersulfated chondroitin sulfate, can also induce anti-PF4/polyanion antibodies with properties similar to those of HIT antibodies.[7,8] Indeed, spontaneous HIT syndrome and fondaparinux-associated HIT can occur in patients with infections or recent major orthopedic surgery, both of which can generate sources of polyanions (such as bacterial surfaces and nucleic acids) from major tissue damage and the breakdown of bacteria, viruses, and blood cells, without any exposure to unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH).[9,10] Because spontaneous HIT syndrome and fondaparinux-associated HIT have been reported most often in patients who have undergone total knee arthroplasty (TKA), major orthopedic surgery itself might be capable of triggering an anti-PF4/heparin immune response.[9] However, the frequency of, and risk factors for, anti-PF4/heparin antibody formation without any heparin exposure remains unclear.

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第43回学会寄稿

抗血小板薬内服中の大腿骨頚部骨折患者に対する人工骨頭挿入術の検討

独立行政法人国立病院機構静岡医療センター

岡本　康義，坪井　義晃，土井　孝信，太田　周介

Safety Evaluation of Hemiarthroplasty for Hip Fracture in Elderly Patients Taking Antiplatelet Agents

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Abstract

Objective: Early operation is considered to have a better outcome for elderly patients with hip fractures. However, elderly patients are often managed on long-term antiplatelet agents/anticoagulant therapy. Therefore, such patients may be at increased risk of perioperative bleeding and other complications. The aim of this study was to evaluate the safety of hemiarthroplasty for hip fracture in patients taking antiplatelet drugs (APDs).

Methods: A retrospective chart review was conducted. Thirty-one patients taking APDs underwent hemiarthroplasty for hip fractures in our hospital between January 2014 and December 2015. All patients had APDs discontinued after admission until two days post-surgery. Patients were divided into two groups, an 'early' group (surgical delay<5 days after admission) or a 'delay' group (surgical delay>4 days after admission). We investigated the patients' hemoglobin (Hb) levels, walking ability, the length of hospitalization, postoperative complications and transfusions associated with APDs.

Results: There was no significant difference with postoperative Hb level and the amount of transfusion between the two groups. There were also no complications related to spinal anesthesia between the two groups. The 'early' group had better walking ability ($P=0.045$) and shorter hospitalization in 9 days ($P=0.024$) compared to the 'delay' group. The 'delay' group significantly increased in the risk of postoperative complications than the 'early' group ($P=0.003$).

Conclusion: There was no significant difference in perioperative bleeding after early hemiarthroplasty in patients taking APDs with hip fractures. Therefore, this study demonstrates that early operation for hip fractures is safe and, in doing so, there may be better outcomes for patients taking such medications.

Keywords: hip fracture, antiplatelet agents, hemiarthroplasty
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The Combined Use of Losartan and Muscle-Derived Stem Cells Significantly Improves the Functional Recovery of Muscle in a Young Mouse Model of Contusion Injuries

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Investigation performed at Stem Cell Research Center, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Background: Although muscle injuries tend to heal uneventfully in most cases, incomplete functional recovery commonly occurs as a result of scar tissue formation at the site of injury, even after treatment with muscle-derived stem cells (MDSCs).

Hypothesis: The transplantation of MDSCs in the presence of a transforming growth factor β1 (TGF-β1) antagonist (losartan) would result in decreased scar tissue formation and enhance muscle regeneration after contusion injuries in a mouse model.

Study Design: Controlled laboratory study.

Methods: An animal model of muscle contusion was developed using the tibialis anterior muscle in 48 healthy mice at 8 to 10 weeks of age. After sustaining muscle contusion injuries, the mice were divided into 4 groups: (1) saline injection group (control group; n = 15), (2) MDSC transplantation group (MDSC group; n = 15), (3) MDSC transplantation plus oral losartan group (MDSC/losartan group; n = 15), and (4) healthy uninjured group (healthy group; n = 3). Losartan was administrated systemically beginning 3 days after injury and continued until the designated endpoint (1, 2, or 4 weeks after injury). MDSCs were transplanted 4 days after injury. Muscle regeneration and fibrotic scar formation were evaluated by histology, and the expression of follistatin, MyoD, Smad7, and Smad2/3 were analyzed by immunohistochemistry and reverse transcription polymerase chain reaction analysis. Functional recovery was measured via electrical stimulation of the peroneal nerve.

Results: When compared with MDSC transplantation alone, MDSC/losartan treatment resulted in significantly decreased scar formation, an increase in the number of regenerating myofibers, and improved functional recovery after muscle contusions. In support of these findings, the expression levels of Smad7 and MyoD were significantly increased in the group treated with both MDSCs and losartan.

Conclusion: When compared with MDSCs alone, the simultaneous treatment of muscle contusions with MDSCs and losartan significantly reduced scar formation, increased the number of regenerating myofibers, and improved the functional recovery of muscle; these effects were caused, at least in part, by the losartan-mediated upregulation of Smad7 and MyoD. Increased levels of Smad7 and MyoD together reduced the deposition of scar tissue (via the inhibition of TGF-β1 by Smad7) and committed the transplanted MDSCs toward a myogenic lineage (via Smad7-regulated MyoD expression).

Clinical Relevance: The study findings contribute to the development of biological treatments to accelerate and improve the quality of muscle healing after injury.

Keywords: stem cells; muscle contusion; muscle injury; scar tissue; fibrosis; losartan; Smad7

Skeletal muscle contusions are among the most common muscle injuries encountered in sports medicine clinics and traumatology.[5] Although the current standard treatments for muscle contusions are typically beneficial, complications such as muscle atrophy, contracture, and fibrotic scar formation at the site of injury may lead to suboptimal clinical outcomes and patient satisfaction.[10,24,25,46] Fibrotic scar formation is perhaps the most detrimental complication that occurs during the healing process and represents an important therapeutic target for the treatment of muscle injuries.[22]

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Negative Association of Diabetes With Thoracic Aortic Dissection and Aneurysm

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Abstract

We performed a meta-analysis to assess the association of diabetes mellitus (DM) with the presence of thoracic aortic dissection (TAD) and/or thoracic aortic aneurysm (TAA). MEDLINE and EMBASE were searched through December 2015 using PubMed and OVID. For each study, data regarding DM prevalence in both the TAD/TAA and control groups were used to generate unadjusted odds ratios (ORs) for DM and 95% confidence intervals (CIs). Alternatively, an unadjusted and/or adjusted OR was directly abstracted from each individual study. Eleven eligible studies enrolling a total of 47 827 participants were included. A primary pooled analysis of all the 11 studies demonstrated that TAD/TAA was associated with significantly lower DM prevalence than controls (OR, 0.43; 95% CI, 0.31-0.59; $P < .00001$). Separate pooled analyses of 6 TAD case studies and 4 TAA case studies demonstrated TAD (OR, 0.34; 95% CI, 0.19-0.61; $P = .0003$) and TAA (OR, 0.65; 95% CI, 0.45-0.94; $P = .02$) were associated with significantly lower DM prevalence than controls. In conclusion, DM may be negatively associated with the presence of TAD/TAA.

Keywords

diabetes mellitus, meta-analysis, thoracic aortic dissection, thoracic aortic aneurysm

Introduction

Although coronary artery disease (CAD) and peripheral artery disease (PAD; both of which are representative atherosclerotic diseases) are positively associated with the presence of abdominal aortic aneurysm (AAA),[1,2] diabetes mellitus (DM, a major risk factor of both CAD and PAD) is negatively associated with not only the presence[3] but also the growth[4] of AAA. The negative association of DM with both the presence[3] and growth[4] of AAA supports the hypothesis that DM may be also negatively associated with the presence of thoracic aortic dissection (TAD) and/or thoracic aortic aneurysm (TAA). However, the association of DM with TAD/TAA has been investigated far less than the association of DM with AAA. Thus, it remains unclear whether DM is negatively associated with TAD/TAA. To summarize the association of DM with the presence of TAD/TAA, we reviewed currently available studies with a systematic literature search and meta-analytic evaluation.

Materials and Methods

All studies reporting the association of DM with the presence of TAD/TAA were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through December 2015 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis. Search terms included diabetes, diabetic, or diabetics and (thoracic) aortic dissection(s) or thoracic aortic aneurysm(s).

Studies considered for inclusion met the following criteria: the design was a case–control study, the study population was patients with TAD/TAA and patients without TAD/TAA, and main outcomes included DM prevalence. For each study, data regarding DM prevalence in both the TAD/TAA and control groups were used to generate unadjusted odds ratio (ORs) for DM and 95% confidence intervals (CIs). Alternatively, an unadjusted and/or adjusted OR for DM with its 95% CI was directly abstracted (as available) from each individual study.

Study-specific estimates (preferentially adjusted estimates) were combined using inverse variance-weighted averages of logarithmic ORs in the random-effects model. Differences in distribution were analyzed using standard χ^2 tests. Sensitivity analyses were performed to assess the contribution of each

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Association of Hypertension with Abdominal Aortic Aneurysm Expansion

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Background: Hypertension is *positively* associated with abdominal aortic aneurysm (AAA) *presence*, which supports a hypothesis that hypertension may also be positively associated with AAA *expansion*. To determine whether hypertension is associated with AAA expansion, we reviewed currently available studies with a systematic literature search and meta-analytic estimate.

Methods: Databases including MEDLINE and EMBASE were searched through July 2015 using Web-based search engines (PubMed and OVID). Studies considered for inclusion met the following criteria: the study population was AAA patients with and without hypertension, and outcomes included data regarding AAA expansion. For each study, expansion rates in both the hypertensive and nonhypertensive groups were used to generate standardized mean differences (SMDs) and 95% confidence intervals (CIs).

Results: Of 614 potentially relevant publications screened initially, we identified 20 eligible studies including data on 6,619 AAA patients. No individual study indicated a statistically significant (positive or negative) association of hypertension with AAA expansion rates. A pooled analysis of all the 20 studies demonstrated that hypertension was not associated with AAA expansion rates in the fixed-effect model (SMD 0.03, 95% CI −0.01 to 0.17, $P = 0.19$). There was no evidence of significant publication bias.

Conclusions: Hypertension is *not* associated with AAA expansion. Further investigations would be required to elucidate why hypertension is not associated with AAA expansion despite its positive association with AAA presence.

INTRODUCTION

Hypertension is *positively* associated with abdominal aortic aneurysm (AAA) *presence*.[1,2] A previous meta-analysis by Cornuz et al.[1] of 9 population-based risk factor studies of AAA showed that hypertension was a risk factor or risk indicator for screening-detected AAA (odds ratio [OR] 1.31, 95% confidence interval [CI] 1.14–1.49). Additionally, a recent meta-analysis by Li et al.[2] of 12 epidemiological studies also showed that hypertension was a risk factor for AAA (OR 1.26, 95% CI 1.15–1.39). These pieces of evidence support a hypothesis that hypertension may also be positively associated with AAA expansion. The RESCAN meta-analysis[3] of individual patient data from 8 studies, however, demonstrated that neither mean blood pressure (BP) nor pulse pressure as continuous data were significantly associated with faster AAA expansion rates (adjusted estimate per 10-mm Hg increase in mean BP 0.013, standard error [SE] 0.021, $P = 0.531$; adjusted estimate per 10-mm Hg increase in pulse pressure −0.027, SE 0.014, $P = 0.060$). To our knowledge, although a lot of studies have reported the association of hypertension as dichotomous data (not BP as continuous data) with AAA expansion, no meta-analysis has been conducted to

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REVIEW

Vitamins and abdominal aortic aneurysm

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ABSTRACT

INTRODUCTION: To summarize the association of vitamins (B6, B12, C, D, and E) and abdominal aortic aneurysm (AAA), we reviewed clinical studies with a comprehensive literature research and meta-analytic estimates.

EVIDENCE ACQUISITION: To identify all clinical studies evaluating the association of vitamins B6/B12/C/D/E and AAA, databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through April 2015, using Web-based search engines (PubMed and OVID). For each case-control study, data regarding vitamin levels in both the AAA and control groups were used to generate standardized mean differences (SMDs) and 95% confidence intervals (CIs).

EVIDENCE SYNTHESIS: Pooled analyses of the 4 case-control studies demonstrated significantly lower circulating vitamin B6 levels (SMD, -0.33; 95% CI, -0.55 to -0.11; P=0.003) but non-significantly lower vitamin B12 levels (SMD, -0.42; 95% CI, -1.09 to 0.25; P=0.22) in patients with AAA than subjects without AAA. Pooled analyses of the 2 case-control studies demonstrated significantly lower levels of circulating vitamins C (SMD, -0.71; 95% CI, -1.23 to -0.19; P=0.007) and E (SMD, -1.76; 95% CI, -2.93 to 0.60; P=0.003) in patients with AAA than subjects without AAA. Another pooled analysis of the 3 case-control studies demonstrated significantly lower circulating vitamin D (25-hydroxyvitamin D) levels (SMD, -0.25; 95% CI, -0.50 to -0.01; P=0.04) in patients with AAA than subjects without AAA. In a double-blind controlled trial, 4.0-year treatment with a high-dose folic acid and vitamin B6/B12 multivitamin in kidney transplant recipients did not reduce a rate of AAA repair despite significant reduction in homocysteine level. In another randomized, double-blind, placebo-controlled trial, 5.8-year supplementation with α-tocopherol (vitamin E) had no preventive effect on large AAA among male smokers.

CONCLUSIONS: In clinical setting, although low circulating vitamins B6/C/D/E (not B12) levels are associated with AAA presence, vitamins B6/B12/E supplementation may not reduce AAA incidence.

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Key words: Aortic aneurysm, abdominal - Review - Vitamins.

The etiological association of some kinds of vitamins with abdominal aortic aneurysm (AAA) has been advocated. First, a meta-analysis by Cao *et al.*[1] and that by us[2] demonstrated that elevated circulating homocysteine levels are associated with AAA presence. Hyperhomocysteinemia can be caused by genetic defects of the enzymes that involved in homocysteine metabolism and/or deficiencies of their co-factors, i.e. folate and vitamins B6/B12.[3] Second, development of oxidative stress through inducible nitric oxide synthesis induction and endothelium dysfunction may contribute to AAA pathologic features.[4-6] To regulate reactive oxygen species production and combat their deleterious effect, the organism responds with a large and complex battery of substances including antioxidants (vitamins A/C/E, carotenoids, and polyphenols).[7] Besides its own free radical activity, vitamin C acts in synergy with α-tocopherol (vitamin E, important chain-breaking lipid-soluble antioxidant) to limit the lipid peroxidation process. Third, vitamin D influences a range of molecular pathways of potential relevance to the pathogenesis of AAA.[8]

Despite the above-mentioned propositions, the association of vitamins with AAA has been clinically investigated far less than other AAA biomarkers in-

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ORIGINAL ARTICLES
CARDIAC SECTION

"Obesity paradox" in transcatheter aortic valve implantation

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ABSTRACT

BACKGROUND: To determine whether body mass index (BMI) is associated with mortality in transcatheter aortic valve implantation (TAVI), we performed a mete-analysis of currently available studies.
METHODS: MEDLINE and EMBASE were searched through September 2015 using PubMed and OVID, to identify all studies investigating an association of BMI with early (in-hospital or 30-day) and mid-term (mean or median follow-up of approximately >6-month) mortality in patients undergoing TAVI.
RESULTS: Our search identified 11 eligible studies including 10,196 patients undergoing TAVI. A pooled analysis of 7 studies (enrolling 4046 patients) reporting a hazard ratio (HR) of BMI as continuous data for mid-term mortality demonstrated that greater BMI was associated with significantly less mid-term mortality (HR per 1-unit increase in BMI, 0.97; 95% confidence interval [CI], 0.94 to 1.00 [0.9982]: P = 0.04). Comparisons of overweight *versus* normal weight and obesity *versus* normal weight for mid-term mortality were not statistically significant. A pooled analysis of 3 studies (enrolling 3901 patients) reporting an odds ratio (OR) of BMI as continuous data for 30-day mortality demonstrated that greater BMI was associated with significantly less mortality (OR per 1-unit increase in BMI, 0.95; 95% CI, 0.92 to 0.98: P = 0.001). Comparisons of overweight *versus* normal weight (P = 0.02) and obesity *versus* normal weight (P = 0.04) for 30-day mortality were statistically significant.
CONCLUSIONS: BMI as continuous data may be associated with better early and mid-term post-TAVI survival. Whereas, overweight or obesity as categorized BMI may be associated with early, not mid-term, post-TAVI survival.

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Key words: Body Mass Index - Meta-analysis - Mortality - Obesity - Transcatheter aortic valve replacement.

Cardiovascular risk factors and left ventricular structure and function are adversely affected by obesity, which is associated with an increase in risk of most cardiovascular disease (CVD).[1] There is, however, an "obesity paradox", *i.e.* obese and/or overweight patients with CVD have a better prognosis than normal-weight patients.[1, 2] Although the obesity paradox could be explained by hypotheses including increased lean body mass, protective peripheral body fat, reduced inflammatory response, genetics, and a decline in CVD risk factors, the paradox would be probably contributed to also by unknown factors.[3] The obesity paradox has been also demonstrated in patients undergoing coronary artery bypass grafting.[4, 5] With respect to surgical aortic valve replacement, however, an association of body mass index (BMI) with mortality has been debated.[6-12] On the other hand, although a number of studies suggest the obesity paradox in patients undergoing transcatheter aortic valve implantation (TAVI), no meta-analysis has been conducted to date. To determine whether BMI is associated with mortality in TAVI, thus, we performed a mete-analysis of currently available studies.

Materials and methods

All eligible studies were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through September 2015

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Direct and adjusted indirect comparisons of perioperative mortality after sutureless or rapid-deployment aortic valve replacement versus transcatheter aortic valve implantation

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ABSTRACT

Objectives: To determine which procedure, aortic valve replacement (AVR) with a sutureless or rapid-deployment prosthesis (SL-AVR) or transcatheter aortic valve implantation (TAVI), achieves better perioperative survival for severe aortic stenosis (AS), we conducted direct-comparison meta-analyses (DC-MAs) and an adjusted indirect-comparison meta-analysis (IDC-MA).

Methods: We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials through April 2016. Eligible studies were randomized controlled trials (RCTs) and propensity-score matched (PSM) studies. We performed a DC-MA-[A] of SL-AVR versus TAVI, a DC-MA-[B] of SL-AVR versus conventional AVR (C-AVR), and a DC-MA-[C] TAVI versus C-AVR. Then, we computed a IDC-MA-[A′] of TAVI versus SL-AVR from the results of the DC-MA-[B] and the DC-MA-[C].

Results: We identified 6 RCTs and 30 PSM studies enrolling a total of 15,887 patients. The 3 DC-MAs demonstrated significantly lower perioperative (30-day or in-hospital) all-cause mortality after SL-AVR than after TAVI (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.28 to 0.80; $p = 0.005$) and no significant differences between SL-AVR and C-AVR (OR, 1.07; 95% CI, 0.60 to 1.94; $p = 0.81$) and between TAVI and C-AVR (1.07; 95% CI, 0.90 to 1.27; $p = 0.45$). The computed IDC-MA-[A′] indicated no significant difference in mortality between SL-AVR and TAVI (1.01; 95% CI, 0.54 to 1.86). Combining the results of the DC-MA-[A] and IDC-MA [A′] showed significantly lower mortality after SL-AVR than after TAVI (OR, 0.65; 95% CI, 0.44 to 0.97; $p = 0.03$).

Conclusions: For patients with severe AS, SL-AVR may achieve better perioperative survival than TAVI.

1. Introduction

Our preliminary meta-analysis [1] suggests that perioperative all-cause mortality is lower after aortic valve replacement (AVR) with a sutureless or rapid-deployment prosthesis (SL-AVR) than after transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS). Statistical power of this meta-analysis [1], however, may be insufficient, because merely 7 observational comparative studies were included in it. Limited or no evidence is often obtained from direct-comparison (DC) studies, and thus an adjusted indirect comparison (IDC) may be required [2]. Additionally, to augment statistical power or precision, it would be possible to quantitatively combine results of the DC and those of the IDC [3]. To determine which procedure, SL-AVR or TAVI, achieves better perioperative overall survival for severe AS, a DC meta-analysis (DC-MA) and an IDC meta-analysis (IDC-MA) were performed, and then results of them were combined.

2. Methods

We identified all randomized controlled trials (RCTs) and propensity-score matched (PSM) studies of SL-AVR versus TAVI, those of SL-AVR versus conventional AVR (C-AVR), and those of TAVI versus C-AVR for severe AS by the use of a 2-level search strategy. First, we searched databases of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials by means of Web-based search engines of PubMed and OVID through April 2016. Second, we identified relevant studies via manual searching secondary sources such as references in articles initially identified, reviews, and commentaries. The following search term were included: *sutureless, rapid-deployment, Enable, Intuity, Perceval,* or *Trilogy*; *percutaneous, transcatheter, transluminal, transarterial, transapical, transaortic,*

Abbreviations: ACC, aortic cross-clamp; AS, aortic stenosis; AVR, aortic valve replacement; C-AVR, conventional AVR; CI, confidence interval; CPB, cardiopulmonary bypass; DC, direct comparison; DC-MA, DC meta-analysis; E/e′, early mitral velocity/annulus velocity; EF, ejection fraction; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HR, hazard ratio; IDC, adjusted indirect comparison; IDC-MA, IDC meta-analysis; OR, odds ratio; PAR, paravalvular aortic regurgitation; PARTNER, Placement of AoRTic TraNscathetER Valves; PMI, pacemaker implantation; PSM, propensity-score matched; RCT, randomized controlled trial; SL-AVR, AVR with a sutureless or rapid-deployment prosthesis; TAVI, transcatheter aortic valve implantation.

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A review of comparative studies of MitraClip versus surgical repair for mitral regurgitation

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Meta-analysis

ABSTRACT

Objectives: We summarized comparative studies of MitraClip versus surgical repair for mitral regurgitation (MR) with a systematic literature search and meta-analytic estimates.

Methods: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through June 2016. Eligible studies were randomized controlled or observational comparative studies of MitraClip versus surgical repair enrolling patients with MR and reporting early (30-day or in-hospital) or late (≥6-month including early) all-cause mortality. For each study, data regarding all-cause mortality and incidence of recurrent >2 + MR in both groups were used to generate odds ratios (ORs). Alternatively, ORs or hazard ratios (HRs) for mortality and recurrent MR themselves were directly abstracted from each study.

Results: Eight reports of 7 studies comparing MitraClip with surgical repair enrolling a total of 1015 patients with MR were identified and included. Pooled analyses demonstrated significantly higher age and logistic European System of Cardiac Operative Risk Evaluation and significantly lower ejection fraction in the MitraClip than surgical repair group, no significant difference in rate of women and patients with New York Heart Association functional class of >II, no statistically significant difference in early- (OR, 0.54; $p = 0.08$) and late-mortality (HR/OR, 1.17; $p = 0.46$), and significantly higher incidence of recurrent MR in the MitraClip than surgical repair group (HR/OR, 4.80; $p < 0.00001$).

Conclusions: In patients with MR, the MitraClip procedure achieves similar survival to surgical MV repair despite higher risk profiles. Recurrent MR, however, occurs more frequently (4.8-fold) after the MitraClip than surgical repair.

1. Introduction

An approximately half number of patients with severe mitral regurgitation (MR) are not treated because of high age, reduced left ventricular function, co-morbidities, or other contraindications to open mitral valve (MV) surgery [1], and accordingly less invasive percutaneous transcatheter MV repair procedures have been developed [2]. The MitraClip-System (Abbott Vascular-Structural Heart, Menlo Park, CA) is an approved system for transcatheter repair, with which both MV leaflets are attached with one or more clips, resulting in a so-called "double-orifice MV" [2]. In high-risk, elderly patients mainly affected by functional MR, the MitraClip procedure is effective with low rates of hospital mortality and adverse events [3]. MitraClip represents an efficacious strategy for patients with heart failure and severe MR and offers a significant improvement in functional class and in cardiac remodeling in patients with severely dilated hearts as well [4]. A number of studies have compared the outcomes of MitraClip with those of surgical repair. We summarized comparative studies of MitraClip versus surgical repair for MR with a systematic literature search and meta-analytic estimates in the present article.

Abbreviations: CI, confidence interval; EF, ejection fraction; EuroSCORE, European System of Cardiac Operative Risk Evaluation; EVEREST, Endovascular Valve Edge-to-Edge Repair Study; HR, hazard ratio; MD, mean difference; MR, mitral regurgitation; MV, mitral valve; OR, odds ratio; NYHA, New York Heart Association; RCT, randomized controlled trial; RD, risk (rate) difference.

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2. Methods

2.1. Search strategy

All studies, including randomized controlled trials (RCTs) and observational comparative studies, of MitraClip versus surgical MV repair enrolling patients with MR were identified using 2-level strategy. First, databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through June 2016 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual

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REVIEW

A meta-analysis of adjusted observational studies and randomized controlled trials of endovascular *versus* open surgical repair for ruptured abdominal aortic aneurysm

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ABSTRACT

INTRODUCTION: The aim of the present meta-analysis was to determine whether endovascular aneurysm repair (EVAR) reduces perioperative mortality and improves overall survival compared with open surgical repair (OSR) in patients with ruptured abdominal aortic aneurysm (RAAA).

EVIDENCE ACQUISITION: Eligible studies were observational studies with adjusted risk estimates or randomized controlled trials (RCTs) of EVAR *versus* OSR enrolling individuals with RAAA and reporting perioperative (30-day or in-hospital) or overall (≥3-month) all-cause mortality.

EVIDENCE SYNTHESIS: Twenty-four adjusted observational studies and 4 RCTs enrolling a total of 56,826 patients with RAAA were identified and included. For perioperative all-cause mortality, pooled analyses of 22 adjusted observational studies and 4 RCTs respectively demonstrated a statistically significant 49% reduction with EVAR relative to OSR (odds ratio [OR]=0.51; 95% confidence interval [CI]: 0.44 to 0.59; P<0.00001) and no statistically significant difference between EVAR and OSR (OR=0.91; 95% CI: 0.68 to 1.22; P=0.53) (P for subgroup differences = 0.0006). For overall (3 months to 8 years) all-cause mortality, a pooled analysis of 7 adjusted observational studies (hazard ratio [HR]=0.92; 95% CI: 0.77 to 1.10; P=0.37) and 3 RCTs (HR=0.89; 95% CI: 0.69 to 1.14; P=0.34) demonstrated no statistically significant difference between EVAR and OSR (P for subgroup differences = 0.81).

CONCLUSIONS: In patients with RAAA, EVAR is likely effective in prevention of perioperative overall (3 months to 8 years), not all-cause mortality.

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Key words: Abdominal aortic aneurysm - Angioplasty - Meta-analysis - Ruptured aneurysm.

Introduction

A recent meta-analysis [1] encompassing 4 randomized controlled trials (RCTs) (Anévrysme de l'aorte abdominale: Chirurgie *versus* Endoprothese [ACE],[2] Dutch Randomized Endovascular AneurysM repair [DREAM],[3] United Kingdom EndoVascular Aneurysm Repair 1 [EVAR 1],[4] and Open *Versus* Endovascular Repair [OVER] [5] trials) with a total of 2783 patients demonstrated that the 30-day all-cause mortality rate was higher with open surgical repair (OSR) than endovascular aneurysm repair (EVAR) for non-ruptured abdominal aortic aneurysm (AAA). However, there was no statistical difference in the long-term all-cause and cause-specific mortality rates between both groups. The authors of a recent systematic Cochrane review [6] including the aforementioned 4 RCTs [2-4] also concluded that EVAR was associated with lower short-term mortality than OSR;

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ORIGINAL ARTICLE

No association of chronic obstructive pulmonary disease with abdominal aortic aneurysm growth

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Abstract Chronic obstructive pulmonary disease (COPD) is independently and positively associated with abdominal aortic aneurysm (AAA) presence. The aim of the present article was to determine whether COPD is associated with AAA growth. We reviewed currently available studies with a systematic literature search and meta-analytic estimate. Databases including MEDLINE and EMBASE were searched through July 2015 using Web-based search engines (PubMed and OVID). Studies considered for inclusion met the following criteria: the study population was AAA patients with and without COPD; and outcomes included data regarding AAA growth. For each study, growth rates in both the COPD and non-COPD groups were used to generate standardized mean differences (SMDs) and 95 % confidence intervals (CIs). Of 614 potentially relevant publications screened initially, we identified 10 eligible studies including data on a total of 2663 AAA patients. None of them demonstrated a statistically significant (positive or negative) association of COPD with AAA growth rates. A pooled analysis demonstrated that COPD is not associated with AAA growth rates (SMD, 0.04; 95 % CI, –0.07 to 0.15; $p = 0.50$). There was no evidence of significant publication bias. In conclusion, we found that COPD is not associated with AAA growth. Further investigations would be required to elucidate why COPD is not associated with AAA growth despite its positive association with AAA presence.

Keywords Abdominal aortic aneurysm · Chronic obstructive pulmonary disease · Meta-analysis

Introduction

In 1985, Cronenwett et al. [1] first identified degree of chronic obstructive pulmonary disease (COPD) as one of risk factors associated with rupture of small abdominal aortic aneurysm (AAA) in patients initially selected for non-operative management. Additionally, a number of studies [2–9] suggest that COPD may be independently and positively associated with AAA presence. For instance, the multivariate logistic regression analysis in a recent case–control (271 and 1387 patients with and without AAA, respectively) study by Song and Park [9] identified COPD as one of the independent predictors for risk of AAA (odds ratio [OR], 1.35; 95 % confidence interval [CI], 1.07–1.72; $p = 0.013$). Also in the multivariate logistic regression analysis of a recent population-based AAA-screening (6142 screened subjects including 469 AAA patients) study by Chun [8], COPD was independently associated with AAA disease (OR, 1.75; 95 % CI, 1.41–2.18; $p < 0.001$). Furthermore, a recent meta-analysis by Li et al. [10] of 6 epidemiological studies also showed that respiratory disease was a risk factor for AAA (OR, 1.36; 95 % CI, 1.19–1.55). These findings regarding the independent and positive association of COPD with AAA presence could hypothesize that COPD may be also positively associated with AAA growth. If COPD is associated with AAA growth, it can be also associated with AAA rupture because AAA growth may be associated with AAA rupture.

For the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group.

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Worse survival after transcatheter aortic valve implantation than surgical aortic valve replacement: A meta-analysis of observational studies with a propensity-score analysis☆

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ABSTRACT

Objectives: To determine whether transcatheter aortic valve implantation (TAVI) improves (or impairs) follow-up overall survival compared with surgical aortic valve replacement (SAVR), we performed a meta-analysis of observational studies with a propensity-score analysis and another meta-analysis of randomized controlled trials (RCTs).

Methods: Databases including MEDLINE and EMBASE were searched through October 2015 using PubMed and OVID. Eligible studies were observational studies with a propensity-score analysis or RCTs of TAVI versus SAVR enrolling patients with severe aortic stenosis and reporting follow-up overall survival or all-cause mortality as an outcome. A hazard ratio (HR) with its 95% confidence interval (CI) of follow-up (including early) all-cause mortality for TAVI versus SAVR was abstracted from each individual study.

Results: Our search identified 19 observational studies with a propensity-score analysis enrolling a total of 6234 patients. The arithmetic means of 1-year and 3-year survival rates were 82.7% and 71.3% after TAVI and 84.8% and 77.9% after SAVR, respectively. A pooled analysis demonstrated a statistically significant 21% increase in the hazard of mortality with TAVI relative to SAVR (HR, 1.21; 95% CI, 1.05 to 1.39; $p = 0.010$). Another pooled analysis of 4 RCTs (enrolling a total of 1795 patients) demonstrated no statistically significant difference in mortality between TAVI and SAVR (HR, 0.92; 95% CI, 0.62 to 1.37; $p = 0.69$).

Conclusions: The arithmetic mean of 3-year survival rates was 71.3% after TAVI and 77.9% after SAVR. Compared with SAVR, TAVI appears to be associated with a significant increase in follow-up all-cause mortality.

1. Introduction

For patients with severe symptomatic inoperable (unsuitable for surgical aortic valve replacement [SAVR]) aortic stenosis (AS), transcatheter aortic valve implantation (TAVI) should be considered. For treatment of inoperable AS, the Placement of Aortic Transcatheter Valves (PARTNER) 1 trial [1] evidently demonstrated that TAVI was more beneficial to late clinical outcomes (survival and functional status) than standard treatment. For patients not inoperable but at moderate-to-high risk for SAVR; however, TAVI is probably unassociated with better early (30-day or in-hospital) all-cause mortality than SAVR [2–7]. Furthermore, in terms of follow-up overall survival (freedom from all-cause mortality), findings of TAVI versus SAVR have been still controversial. To our best knowledge with a systematic literature search, 4 randomized controlled trials (RCTs) [8–11] reported follow-up results. One RCT demonstrated significantly better follow-up overall survival in TAVI [10], another did significantly better survival in SAVR [9], and the other 2 did no significant difference in survival between TAVI and SAVR [8,11]. Although a lot of observational comparative studies have been conducted, results should be always interpreted with caution when they are included in meta-analyses because of greater potential biases for non-randomized studies compared with RCTs [12]. Particular concerns arise with respect to differences between patients in different intervention groups (selection bias). Unlike for RCTs, it would usually be appropriate to analyze adjusted (rather than unadjusted) effect estimates, i.e., analyses that attempt to control for confounding [12]. A

Abbreviations: AS, aortic stenosis; CABG, coronary artery bypass grafting; CI, confidence interval; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HR, hazard ratio; LV, left ventricle; LVEF, LV ejection fraction; NOTION, Nordic Aortic Valve Intervention; OR, odds ratio; PAR, paravalvular aortic regurgitation; PARTNER, Placement of Aortic Transcatheter Valves; PMI, permanent pacemaker implantation; RCT, randomized controlled trial; RR, risk ratio; SAVR, surgical aortic valve replacement; STACCATO, prospective, randomized trial of transapical transcatheter aortic valve implantation vs. surgical aortic valve replacement in operable elderly patients with aortic stenosis; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVI, transcatheter aortic valve implantation.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Original Article

Negative association of diabetes with rupture of abdominal aortic aneurysm

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Hisato Takagi and Takuya Umemoto; for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

Abstract

Purpose: To summarize the association of diabetes with abdominal aortic aneurysm rupture, we reviewed currently available studies with a systematic literature search and meta-analytic evaluation.

Methods: To identify all studies reporting the association of diabetes with abdominal aortic aneurysm rupture, MEDLINE and EMBASE were searched through July 2015. For each study, data regarding diabetes prevalence in both the ruptured and non-ruptured groups were used to generate an unadjusted odds ratio for abdominal aortic aneurysm rupture and 95% confidence intervals. Alternatively, an unadjusted or adjusted odds ratio, or hazard ratio for abdominal aortic aneurysm rupture with 95% confidence interval was directly abstracted (as available) from each individual study.

Results: Our search identified 11 eligible studies. A primary meta-analysis of nine studies reporting data on ruptured (not including non-ruptured symptomatic) abdominal aortic aneurysm demonstrated that diabetes was associated with significantly lower prevalence/incidence of abdominal aortic aneurysm rupture (odds ratio/hazard ratio, 0.71; 95% confidence interval, 0.56 to 0.89; $p=0.003$). A secondary meta-analysis of all 11 studies (adding two studies in which non-ruptured symptomatic abdominal aortic aneurysm was included in the rupture group) also demonstrated that diabetes was associated with significantly lower prevalence/incidence of abdominal aortic aneurysm rupture (odds ratio/hazard ratio, 0.77; 95% confidence interval, 0.63 to 0.95; $p=0.01$).

Conclusion: Diabetes is negatively associated with abdominal aortic aneurysm rupture.

Keywords

Abdominal aortic aneurysm, diabetes, meta-analysis, rupture

Introduction

Coronary artery disease (CAD) and peripheral artery disease (PAD), both representative atherosclerotic diseases, are positively associated with the presence of abdominal aortic aneurysm (AAA).[1,2] Despite the positive associations of CAD and PAD with AAA presence, diabetes (major risk factor of CAD and PAD) is negatively associated with not only presence[3] but also growth[4] of AAA. The negative associations of diabetes with AAA presence and growth support the hypothesis that diabetes may be also negatively associated with AAA rupture. The RESCAN individual patient data meta-analysis[5] of only two studies[6,7] including a total of 3153 patients with small AAA, however, revealed no association between diabetes and rupture. Whereas, a recent large (including 188 patients with ruptured and 1482 patients with non-ruptured AAA) retrospective study by Theivacumar et al.[8] suggests that diabetes patients with AAA are significantly less likely to present with rupture or to die from aneurysm rupture when compared to non-diabetes patients with AAA. It is still debated whether diabetes is negatively associated with AAA rupture. To summarize the association of diabetes with AAA rupture, we reviewed currently available studies with a systematic literature search and meta-analytic evaluation in this article.

Methods

All studies reporting the association of diabetes with AAA rupture were identified using a two-level search strategy. First, databases including MEDLINE and EMBASE were searched through July 2015 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles

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Original article

Overweight, but not obesity, paradox on mortality following coronary artery bypass grafting

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ABSTRACT

Objectives: To determine whether an "obesity paradox" on post-coronary artery bypass grafting (CABG) mortality exists, we abstracted exclusively adjusted odds ratios (ORs) and/or hazard ratios (HRs) for mortality from each study, and then combined them in a meta-analysis.

Methods: MEDLINE and EMBASE were searched through April 2015 using PubMed and OVID, to identify comparative studies, of overweight or obese versus normal weight patients undergoing CABG, reporting adjusted relative risk estimates for short-term (30-day or in-hospital) and/or mid-to-long-term all-cause mortality.

Results: Our search identified 14 eligible studies. In total our meta-analysis included data on 79,140 patients undergoing CABG. Pooled analyses in short-term mortality demonstrated that overweight was associated with a statistically significant 15% reduction relative to normal weight (OR, 0.85; 95% confidence interval [CI], 0.74–0.98; $p = 0.03$) and no statistically significant differences between mild obesity, moderate/severe obesity, or overall obesity and normal weight. Pooled analyses in mid-to-long-term mortality demonstrated that overweight was associated with a statistically significant 10% reduction relative to normal weight (HR, 0.90; 95% CI, 0.84 to 0.96; $p = 0.001$); and no statistically significant differences between mild obesity, moderate/severe obesity, or overall obesity and normal weight.

Conclusions: Overweight, but not obesity, may be associated with better short-term and mid-to-long-term post-CABG survival relative to normal weight. An overweight, but not obesity, paradox on post-CABG mortality appears to exist.

Introduction

Cardiovascular risk factors and left ventricular structure and function are adversely affected by obesity, which is associated with an increase in risk of most cardiovascular disease (CVD) [1]. There is, however, an "obesity paradox," i.e. obese and overweight patients with CVD have a better prognosis than normal weight patients with CVD [1]. A recent study by Banack and Kaufman [2], using data from 17,636 participants in the US National and Nutrition Examination Survey, reported that the adjusted risk ratio (RR) relating obesity and all-cause mortality was 1.24 [95% confidence interval (CI), 1.11 to 1.39] in the general population. The adjusted RR comparing the obese and the non-obese was 0.79 (95% CI, 0.68 to 0.91) among subjects with CVD and 1.30 (95% CI, 1.12 to 1.50) among subjects without CVD, indicating that obesity is protectively associated with mortality among patients with CVD (which, however, can be explained by a simple selection bias) [2]. In addition, the obesity paradox has been demonstrated in patients undergoing cardiac and non-cardiac surgery. Although the obesity paradox could be explained by hypotheses including increased lean body mass, protective peripheral body fat, reduced inflammatory response, genetics, and a decline in CVD risk factors, the paradox would be probably contributed to also by unknown factors [3]. In a previous (published in 2008) meta-analysis by Oreopoulos et al. [4] of 12 cohort publications reporting results in post-coronary artery bypass grafting (CABG) populations, obese patients had lower short-term [odds ratio (OR), 0.63; 95% CI, 0.56 to 0.71] and similar long-term (OR, 0.88; 95% CI, 0.60 to 1.29) mortality risk compared to normal weight patients, and results were similar in overweight patients. The authors [4] abstracted

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Association of peripheral artery disease with abdominal aortic aneurysm growth

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Objective: **To determine whether an association of peripheral artery disease (PAD) with abdominal aortic aneurysm (AAA) growth is positive, none, or negative, a meta-analysis of all available studies was performed through a systematic literature search.**

Methods: **MEDLINE and Embase databases were searched until July 2015 by the use of PubMed and Ovid Web-based search engines. The search terms were enlargement, expansion, growth, or progression; and abdominal aortic aneurysm. Studies that fulfilled the following criteria were included: (1) AAA patients with PAD and those without PAD as the population and (2) data of AAA growth as the outcomes. By means of growth rates in patients with and without PAD for each study, we generated standardized mean differences (SMDs) and their 95% confidence intervals (CIs).**

Results: **Of 612 initially screened publications that were potentially relevant, 11 eligible studies that reported the correlation between PAD and AAA growth were identified, and a total of 4573 patients with AAA were included. A pooled analysis of the 11 studies demonstrated a statistically significant association of PAD with lower growth rates of AAA (SMD, −0.18; 95% CI, −0.25 to −0.11; $P < .00001$). In addition, separately combining seven adjusted effect estimates did not substantively alter the pooled estimate (SMD, −0.17; 95% CI, −0.25 to −0.09; $P < .0001$). No significant publication bias was observed.**

Conclusions: **PAD is likely negatively associated with AAA growth. Further research is required to explain why PAD *negatively* correlates with AAA *growth* despite a *positive* correlation with AAA *presence*. (J Vasc Surg 2016;64:506-13.)**

The first (published in 2004) meta-analysis by Cornuz et al[1] of eight population-based studies of abdominal aortic aneurysm (AAA) showed that peripheral artery disease (PAD) is a major risk factor or indicator for AAA detected in screening. Another recent (published in 2013) meta-analysis by Li et al[2] of three epidemiologic studies also showed claudication is a risk factor for AAA. Despite the *positive* correlation between PAD and AAA *presence*,[1,2] there may be *no* association[3]—or a *negative* association[4]—with AAA *growth*. Bhak et al[3] used a large database from the Aneurysm Detection and Management (ADAM) study and found no association of claudication with expansion rates of AAA. Unexpectedly, a longitudinal study from the UK Small Aneurysm Trial (UKSAT) by Brady et al[4] demonstrated that more severe PAD (ie, lower ankle-brachial pressure index) was associated with slower growth rates of AAA, which means a negative correlation between PAD and AAA growth.

These data suggest a minimal role of atherosclerosis in the continuous expansion of AAA, which is a character of its natural history.[4] Although AAA has traditionally been considered to follow atherosclerosis, recent findings support the concept of AAA growth by way of pathologic mechanisms different from those that bring about atherosclerotic occlusive disease.[5,6] To determine whether an association of PAD with AAA growth is positive, none, or negative, a meta-analysis of all available studies was performed through a systematic literature search.

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METHODS

Search strategy. We used a two-level search strategy to identify all studies that reported growth rates of AAA. First, we searched MEDLINE and Embase databases until July 2015 by the use of the PubMed and Ovid Web-based search engines. Second, we identified relevant studies by manually searching secondary sources, such as references of articles initially identified, reviews, and commentaries, and downloaded all references to eliminate duplicates and to consolidate and further analyze them. The following search terms were included: enlargement, expansion, growth, or progression; *and* abdominal aortic aneurysm.

Study selection and data abstraction. Studies were included when they fulfilled the following criteria: (1) AAA patients with and without PAD as the population and (2) data of AAA growth as the outcome. We included the following data of AAA growth: (1) growth rates in patients with and without PAD, (2) mean differences (MDs) between growth rates in patients with and without PAD, (3) proportions of PAD patients with rapid AAA growth and those with slow AAA growth (according to the definition by the authors of each study), or (4) odds ratios (ORs) of PAD for rapid growth of AAA or for slow growth of AAA.

A Meta-Analysis of Sutureless or Rapid-Deployment Aortic Valve Replacement

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Abstract

Objective To summarize the safety of sutureless or rapid-deployment aortic valve replacement (AVR), we performed a systematic review and meta-analysis of single-arm studies.

Methods MEDLINE and EMBASE were searched through December 2014. Studies considered for inclusion met the following criteria: the design was a single-arm study enrolling ≥50 participants; the study population consisted of patients undergoing sutureless/rapid-deployment AVR; and main outcomes included early (in-hospital or 30-day) mortality and/or overall survival.

Results Of 250 potentially relevant articles screened initially, 11 eligible studies enrolling a total of 2,066 patients were identified and included. The Enable, Intuity, and Perceval bioprostheses were used in three, two, and six studies, respectively. Mean age of patients was 77.6 years, and 56.9% of patients were women. Mean logistic European System for Cardiac Operative Risk Evaluation I and II were 10.5 and 7.4%, respectively. Aortic cross-clamp times in overall patients, patients undergoing isolated AVR, those undergoing AVR with any concomitant procedures, and those undergoing AVR with coronary artery bypass grafting were 44.7, 41.9, 56.2, and 51.3 minutes, respectively. Arithmetic mean of early mortality was 2.6%, and fixed-effects combined early mortality was 3.2% (95% confidence interval, 2.5–4.2%). Arithmetic mean of 1-year survival was 89.7%, and fixed-effects combined 1-year mortality was 10.4% (9.0–12.1%).

Conclusion Sutureless/rapid-deployment AVR is feasible and safe with approximate 3 and 10% of early and 1-year mortality, respectively. Large-size randomized controlled trials, however, are needed to determine whether sutureless/rapid-deployment AVR improves mortality compared with conventional AVR.

Keywords
- meta-analysis
- rapid-deployment aortic valve replacement
- sutureless aortic valve replacement

Introduction

Magovern and Cromie[1] came up with the concept of sutureless aortic valve in the early 1960s when they designed a ball cage–type mechanical valve for sutureless implantation.[2] This valve continued to be used till 1980 but had some disadvantages, especially high incidence of perivalvular leaks. With the advent of transcatheter aortic valve implantation (TAVI) techniques, a renewed interest has developed in sutureless aortic valve concepts in the last decade.[2] Speedy insertion, which is the main feature of sutureless aortic prosthesis, makes implantation easier for surgeons and may reduce cross-clamp times and myocardial ischemia. Three different sutureless or rapid-deployment bioprostheses are currently approved for clinical use in Europe: the Enable sutureless

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Impact of paravalvular aortic regurgitation after transcatheter aortic valve implantation on survival☆

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ABSTRACT

Objectives: To determine whether ≥moderate paravalvular aortic regurgitation (PAR) after transcatheter aortic valve implantation (TAVI) independently impairs overall survival and how much the impact on survival is, we performed an updated meta-analysis pooling not unadjusted but adjusted hazard ratios (HRs).
Methods: Databases including MEDLINE and EMBASE were searched through January 2016 using PubMed and OVID. Search terms included *paravalvular* or *perivalvular*; *regurgitation*, *leak*, or *leakage*; *percutaneous*, *transcatheter*, *transluminal*, *transarterial*, *transapical*, *transaortic*, *transcarotid*, *transaxillary*, *transsubclavian*, *transiliac*, *transfemoral*, or *transiliofemoral*; and *aortic valve*. Studies considered for inclusion met the following criteria: the design was an observational comparative study; the study population was patients undergoing TAVI; patients were divided into ≥moderate and ≤mild post-TAVI PAR; outcomes included ≥1-year all-cause mortality; and the adjustment method was a multivariate Cox proportional hazards analysis. An adjusted HR with its 95% confidence interval (CI) for ≥moderate post-TAVI PAR was abstracted from each individual study.
Results: Our search identified 17 eligible studies including a total of 15,131 patients. A pooled analysis of all the 17 studies demonstrated a statistically significant 2.12-fold increase in mortality with ≥moderate PAR (HR, 2.12; 95% CI, 1.79 to 2.51; $p < 0.00001$). Exclusion of any single study from the meta-analysis did not substantively alter the overall result disfavoring ≥moderate PAR. Although the statistical tests suggested funnel plot asymmetry, the corrected effect estimate from the trim-and-fill method demonstrated still a statistically significant 1.83-fold risk of mortality with ≥moderate PAR.
Conclusions: ≥Moderate post-TAVI PAR is associated with a 2.12-fold increase in overall (≥1-year) all-cause mortality.

1. Introduction

The incidence of moderate or severe (≥moderate) paravalvular aortic regurgitation (paravalvular AR, PAR) after transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS) has been reported to be 12–21% [1], which is approximately 6-fold higher than that after surgical aortic valve replacement (SAVR) [2]. A number of studies suggest that ≥moderate PAR is an independent risk factor of overall mortality. However, some investigators [3,4] demonstrated a significant >4-fold risk, whereas other researchers [5,6] indicated a non-significant <2-fold risk. Only one previous (published in 2013) meta-analysis [7] of 9 studies [8–16] demonstrated a 2.27-fold risk of 1-year mortality for ≥moderate PAR. The meta-analysts [7], however, abstracted (then pooling in a meta-analysis) "adjusted" (using a "multivariate" analysis) hazard ratios (HRs) from only 3 studies [9,10,16] and "unadjusted" (using a "univariate" analysis) HRs from the other 6 studies [8,11–15]. One [16] of the 3 adjusted HRs was for not overall (including early) but only late (not including early) mortality. Furthermore, of the 6 unadjusted HRs, one [8] was for not all-cause but cardiovascular mortality, and another [13] for not ≥moderate (not including mild) but no/trace or mild (≤mild) (including mild) PAR. Unadjusted results of observational studies should be always interpreted with caution when they are included in meta-analyses because of greater potential biases compared with adjusted results. Particular concerns arise with respect to differences between patients in different groups (selection bias). It would usually be appropriate to analyze adjusted (rather than unadjusted) effect estimates, i.e. analyses that attempt to control for confounding [17]. To

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; CI, confidence interval; HR, hazard ratio; LV, left ventricle; MR, mitral regurgitation; OR, odds ratio; PAR, paravalvular AR; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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A Meta-Analysis of the Association of Chronic Obstructive Pulmonary Disease with Abdominal Aortic Aneurysm Presence

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Background: Several case–control and population-based abdominal aortic aneurysm (AAA) screening studies have reported inconclusive results of the association of chronic obstructive pulmonary disease (COPD) with AAA presence. To determine whether COPD is associated with AAA presence, we performed a meta-analysis of contemporary clinical studies.

Methods: To identify all contemporary case–control and population-based AAA screening studies evaluating the association of COPD with AAA presence, databases including MEDLINE and EMBASE were searched from January 2000 to May 2015 using Web-based search engines (PubMed and OVID). An adjusted odds ratio (OR) and 95% confidence intervals (CI) for COPD or AAA presence (using multivariable logistic regression) were abstracted from each individual study. We took an OR for AAA presence to be representative of an OR for COPD presence.

Results: Of 159 potentially relevant articles screened initially, there were 7 case–control and 4 population-based AAA screening studies that met eligibility requirements and were included. Pooled analysis of all the 11 studies (14 estimates, 155,731 participants), 7 case–control studies (4171 participants), and 4 population-based AAA screening studies (7 estimates, 151,560 participants) respectively demonstrated a statistically significant 1.78-fold (OR 1.78, 95% CI 1.38–2.30, $P < 0.00001$), 3.05-fold (OR 3.05, 95% CI 1.44–6.49, $P = 0.004$), and 1.24-fold (OR 1.24, 95% CI 1.04–1.48, $P = 0.02$) increased prevalence/incidence of COPD in patients with AAA relative to subjects without AAA (i.e., a statistically significant 1.78-, 3.05-, and 1.24-fold increased prevalence/incidence of AAA in patients with COPD relative to subjects without COPD) (P for subgroup differences = 0.02).

Conclusion: The present meta-analysis demonstrated 1.8-fold increased prevalence/incidence of COPD in patients with AAA relative to subjects without AAA (i.e., 1.8-fold increased prevalence/incidence of AAA in patients with COPD relative to subjects without COPD), which suggests that COPD is associated with AAA presence.

INTRODUCTION

Between abdominal aortic aneurysm (AAA) and chronic obstructive pulmonary disease (COPD), there are several parallels regarding both risk factors and underlying pathophysiology.[1] A particularly strong relationship with smoking is observed in both AAA and COPD. Furthermore, the principal disease-modifying intervention of both diseases is likely to be smoking cessation.[1] An aggressive smoking intervention program significantly reduces the age-related decline in forced expiratory volume in 1 sec in middle-aged smokers with mild airways obstruction.[2] Smoking cessation also reduces

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Diabetes and Abdominal Aortic Aneurysm Growth

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Abstract

We performed a systematic literature search and a meta-analysis to assess the association between diabetes mellitus (DM) and abdominal aortic aneurysm (AAA) growth. Databases including MEDLINE and EMBASE were searched through June 2015 using PubMed and OVID. For each study, data regarding AAA growth rates in both the DM and the non-DM groups were used to generate standardized mean differences (SMDs) and 95% confidence intervals (CIs). Our search identified 19 relevant studies including data on 9777 patients with AAA. Pooled analyses demonstrated a statistically significant slower growth rates in DM patients than in non-DM patients (unadjusted SMD, −0.32; 95% CI, −0.40 to −0.24; $P < .00001$; adjusted SMD, −0.29; 95% CI, −0.417 to −0.18; $P < .00001$). Despite possible publication bias in favor of DM based on funnel plot asymmetry, even adjustment of the asymmetry did not alter the beneficial effect of DM. In conclusion, on the basis of a meta-analysis of data on a total of 9777 patients (19 studies) identified through a systematic literature search, we confirmed the association of DM with slower growth rates of AAA.

Keywords

abdominal aortic aneurysm, aneurysm growth, diabetes mellitus, meta-analysis

Introduction

Our recent meta-analysis[1] of adjusted relative risk estimates from 13 studies including data on >3 800 000 participants confirmed that diabetes mellitus (DM) is inversely associated with the presence of abdominal aortic aneurysm (AAA), and this supports the hypothesis that DM may be negatively associated with AAA growth. The RESCAN meta-analysis[2,3] showed that growth rates of small (3.0-5.5 cm) AAA were decreased in patients with DM. The RESCAN collaborators identified 25 studies for potential inclusion. Although requests for individual patient data (IPD) were addressed to the corresponding authors of these studies, data were not available from 7 studies, and accordingly the collaborators provided data from 18 studies. A meta-analysis of 6268 IPD from 10 studies (of the available 18 studies) demonstrated that DM patients had growth rates that were on average 0.51 (standard error [SE], 0.10) mm/year slower than those of non-DM patients after adjustment for all demographics, medical history, and drug history. Medical evidence, however, should be based on a systematic review with a quantitative meta-analysis of as many relevant studies as possible identified through a systematic literature search rather than on narrative reviews of voluntarily selected studies. Systematic reviews require a thorough, objective, and reproducible search of a range of sources to identify as many studies as possible (within resource limits), which is a major factor in distinguishing systematic reviews from narrative reviews and helps to minimize bias and therefore assist in achieving reliable estimates of the effects.[4] To assess the association between DM and AAA growth, we performed a meta-analysis with a systematic literature search.

Materials and Methods

Search Strategy

All studies reporting AAA growth rates in patients with and without DM were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through June 2015 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis. Search

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Coronary artery disease and abdominal aortic aneurysm growth

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Abstract

To determine whether coronary artery disease (CAD) is associated with abdominal aortic aneurysm (AAA) growth, we performed a meta-analysis of currently available studies. Databases including MEDLINE and EMBASE were searched through October 2015 using PubMed and OVID. Search terms included *enlargement, expansion, growth*, or *progression; rate* or *rates*; and *abdominal aortic aneurysm*. Studies considered for inclusion met the following criteria: the design was unrestricted; the study population was AAA patients with and without CAD; and outcomes included data regarding AAA growth. For each study, growth rates in both the CAD and non-CAD groups were used to generate standardized mean differences (SMDs) and 95% confidence intervals (CIs). Of 664 potentially relevant publications screened initially, we identified 20 eligible studies including data on a total of 7238 AAA patients. A pooled analysis of all 20 studies demonstrated a statistically significant association of CAD with slower AAA growth rates (i.e. a significantly negative association of CAD with AAA growth) in the fixed-effect model (SMD, –0.06 [–0.0592]; 95% CI, –0.12 [–0.1157] to –0.00 [–0.0027]; $p = 0.04$). There was minimal between-study heterogeneity ($p = 0.16$) and a statistically non-significant association of CAD with slower AAA growth rates (i.e. a non-significantly negative association of CAD with AAA growth) in the pooled result from random-effects modeling (SMD, –0.06; 95% CI, –0.13 to 0.01; $p = 0.12$). In conclusion, CAD may be negatively associated with AAA growth.

Keywords

abdominal, aortic aneurysm, coronary disease, epidemiology, meta-analysis

Introduction

The first (published in 2004) meta-analysis by Cornuz et al.[1] of six population-based risk factor studies of abdominal aortic aneurysm (AAA) showed that a history of coronary artery disease (CAD) was a major risk factor or risk indicator for screening-detected AAA (odds ratio [OR], 2.30; 95% confidence interval (CI), 1.92 to 2.75). Another recent (published in 2013) meta-analysis by Li et al.[2] of three epidemiological studies also showed that CAD was a risk factor for AAA (OR, 1.82; 95% CI, 1.65 to 2.00). Despite the evidence for the *positive* association of CAD with AAA *presence*, however, CAD may be *not*[3] or even *negatively*[4] associated with AAA *growth*. Using a large clinical database from the ADAM (Aneurysm Detection and Management) study, Bhak et al.[3] found no association between angina or CAD and AAA expansion rates. Unexpectedly, in a retrospective cohort study, Nakayama et al.[4] demonstrated an inverse association between the existence of CAD and an accelerated AAA expansion rate (i.e. negative association of CAD with AAA growth) in 510 elective repair cases for which at least two follow-up CT scans of AAA were available. These data suggest that atherosclerosis has a minimal role in the continuing expansion that characterizes the natural history of AAA.[5] Although AAA has been traditionally regarded as a consequence of atherosclerosis, recent findings lend support to the concept that AAA grows through pathologic mechanisms that differ from those responsible for atherosclerotic occlusive disease.[4,6,7] To determine whether CAD is associated with AAA growth, we performed a meta-analysis of currently available studies.

Methods

All studies reporting AAA growth rates were identified using a two-level search strategy. First, databases including

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Original article

Sutureless aortic valve replacement may improve early mortality compared with transcatheter aortic valve implantation: A meta-analysis of comparative studies

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ABSTRACT

Objectives: To determine which improves clinical outcomes more, sutureless (including rapid-deployment) aortic valve replacement (AVR) or transcatheter aortic valve implantation (TAVI), we performed a meta-analysis of comparative studies.

Methods: MEDLINE and EMBASE were searched through June 2015 using Web-based search engines (PubMed and OVID). Studies considered for inclusion met the following criteria: the design was a comparative study; the study population included patients with severe aortic valve stenosis, patients were assigned to sutureless AVR versus TAVI; and main outcomes included at least early (in-hospital or 30-day) all-cause mortality.

Results: Of 87 potentially relevant articles screened initially, no randomized controlled trials and 7 observational comparative studies of sutureless AVR versus TAVI (enrolling a total of 945 patients) were identified and included. The first pooled analysis demonstrated a statistically significant reduction in mortality with sutureless AVR over TAVI [2.5% versus 7.3%; odds ratio (OR), 0.33; 95% confidence interval (CI), 0.16 to 0.69; $p = 0.003$; risk difference (RD), −5.23%; 95% CI, −8.12% to −2.33%; $p = 0.0004$]. The second pooled analyses demonstrated no statistically significant difference in bleeding complications, acute kidney injury, and conduction disturbance between sutureless AVR and TAVI. The third pooled analysis demonstrated a statistically significant reduction in paravalvular aortic regurgitation (AR) with sutureless AVR over TAVI (3.5% versus 33.2%; OR, 0.09; 95% CI, 0.05 to 0.16, $p < 0.00001$; MD, −22.56%; 95% CI, −36.59% to −8.53%; $p = 0.002$).

Conclusions: Compared with TAVI, sutureless AVR may be associated with a reduction in early mortality and postoperative paravalvular AR.

Introduction

In the early 1960s, Magovern and Cromie [1] designed a ball-cage-type mechanical valve with the concept of sutureless aortic valve implantation. Although this valve continued to be used until 1980, it had some disadvantages especially a high incidence of paravalvular leaks [2]. With the advent of transcatheter aortic valve implantation (TAVI) techniques, a renewed interest has developed in sutureless aortic valve concepts in the last decade. Speedy insertion, which is the main feature of sutureless aortic prosthesis, makes implantation easier for surgeons and may reduce cross-clamp times and myocardial ischemia [2]. Three different sutureless (including rapid-deployment) bioprostheses are currently approved for clinical use in Europe: the Enable sutureless (Medtronic Inc, Minneapolis, MN, USA), the Intuity rapid-deployment (Edwards Lifesciences Corp, Irvine, CA, USA), and the Perceval sutureless (Sorin Biomedica Cardio Srl, Sallugia, Italy) valves. Although results of dozens of single-arm studies of sutureless aortic valve replacement (AVR) have been published to date, there have been no randomized controlled trials and only a limited number of observational comparative studies of sutureless AVR versus TAVI. It remains, hence, unclear which improves clinical outcomes more, sutureless AVR or TAVI. To determine this,

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Original article

A meta-analysis of case-control studies of the association of migraine and patent foramen ovale

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ABSTRACT

Objectives: To establish quantitative evidence, we performed the first meta-analysis of case-control studies assessing the relationship between migraine and patent foramen ovale (PFO).
Methods: MEDLINE and EMBASE were searched through April 2015 using PubMed and OVID. Eligible studies were case-control studies reporting PFO (or migraine) prevalence in migraine patients versus no-migraine subjects (or PFO patients versus no-PFO subjects).
Results: Of 395 potentially relevant articles screened initially, 21 eligible studies enrolling a total of 5572 participants were identified and included. Pooled analyses demonstrated statistically significant 3.36-fold migraine-with-aura [odds ratio (OR), 3.36; 95% confidence interval (CI), 2.04–5.55; $p < 0.00001$] and 2.46-fold migraine-with/without-aura prevalence (OR, 2.46; 95% CI, 1.55–3.91; $p = 0.0001$) but statistically non-significant 1.30-fold migraine-without-aura prevalence (OR, 1.30; 95% CI, 0.85–1.99; $p = 0.22$) in PFO patients relative to no-PFO subjects.
Conclusions: PFO is associated with 3.4-fold migraine-with-aura and 2.5-fold migraine-with/without-aura prevalence but unassociated with migraine-without-aura prevalence.

Introduction

Migraine and patent foramen ovale (PFO) may be associated with each other, although the precise pathophysiological mechanisms are uncertain. A recent systematic review [1] summarized findings from 8 case-control studies enrolling approximately 1600 participants and showed 16.0–25.7% of PFO prevalence in the controls, 26.8–96.0% for migraine-with-aura patients, and 22.6–72.4% for migraine-without-aura patients. On the other hand, a number of investigators have recently argued that there is no association between migraine and PFO [2–4]. Further, as far as we know, no meta-analyses have quantitatively confirmed the association of migraine and PFO. To establish quantitative evidence, we performed the first meta-analysis of case-control studies assessing the relationship between migraine and PFO.

Methods

All eligible studies were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through April 2015 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. Search terms included *migraine* and *foramen ovale*.

Studies considered for inclusion met the following criteria: the design was a case-control study; the study population was (1) patients with migraine and subjects without migraine or (2) patients with PFO and subjects without PFO; and main outcomes included prevalence of (1) PFO or (2) migraine. Exclusion criteria were studies investigating an association between migraine and ischemic stroke (mentioned in a previous meta-analysis by Davis et al. [2]) and studies evaluating migraine after percutaneous closure of PFO (addressed in another previous meta-analysis by Butera et al. [3]).

For each study, data regarding (1) PFO prevalence in both the migraine and no-migraine groups or (2) migraine prevalence in both the PFO and no-PFO groups were used to generate unadjusted

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REVIEW
CARDIAC SECTION

Seizures associated with tranexamic acid for cardiac surgery: a meta-analysis of randomized and non-randomized studies

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ABSTRACT

INTRODUCTION: The aim of this meta-analysis was to assess whether tranexamic acid (TXA) therapy for adult cardiac surgery is associated with an increase in the risk of seizures and performed a meta-analysis of randomized controlled trials (RCTs) and non-randomized observational studies.

EVIDENCE ACQUISITION: MEDLINE and EMBASE were searched through December 2016 using PubMed and OVID. Eligible studies were RCTs and non-randomized observational studies on TXA *versus* control (no TXA, placebo, or active control such as low-dose TXA, aprotinin, and epsilon aminocaproic acid) enrolling adult patients undergoing cardiac surgery and reporting the postoperative incidence of seizures as an outcome. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic odds ratios in the random-effects model.

EVIDENCE SYNTHESIS: Of 90 potentially relevant articles screened initially, 16 reports of eligible studies were identified and included. A pooled analysis of all 16 studies (enrolling 45,235 patients) demonstrated that TXA therapy was associated with a statistically significant increase in the seizures incidence (OR=4.13; 95% CI: 2.59 to 6.57; P<0.00001). A subgroup analysis indicated a statistically significant increase in the seizures incidence with TXA therapy in all subgroups of 5 RCTs, 5 adjusted observational studies, and 6 unadjusted observational studies with no statistically significant subgroup differences (P=0.36; I^2=1.5%).

CONCLUSIONS: The results of the present meta-analysis of 16 studies enrolling 45,235 patients confirmed that TXA therapy for adult cardiac surgery is associated with a 4.1-fold increase in the risk of seizure.

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Introduction

In patients undergoing cardiac surgery, antifibrinolytic agents (including aprotinin and the lysine analogues tranexamic acid [TXA] and epsilon aminocaproic acid [EACA]) have been used and reduce the risk of blood loss and transfusion. These agents which may have prothrombotic effects, however, may potentially increase the risk of myocardial infarction, stroke, and other thrombotic complications after cardiac surgery. TXA, a synthetic analogue of the amino acid lysine, is an effective blood-conserving agent with significantly lower risk of death and possibly a lower propensity to cause postoperative myocardial infarction than aprotinin which has now been withdrawn from routine clinical practice, whereas its indiscriminate use and inconsistent dosing regimens can potentially increase the likelihood of postoperative neurological complications especially

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Worse late-phase survival after elective endovascular than open surgical repair for intact abdominal aortic aneurysm

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ABSTRACT

Objectives: To determine whether follow-up survival is better after elective endovascular aneurysm repair (EVAR) than open surgical repair (OSR) for intact abdominal aortic aneurysm (AAA), we combined 5-year survival curves themselves of EVAR and OSR in randomized controlled trials (RCTs) and propensity-score matched (PSM) studies.

Methods: Eligible studies were RCTs or PSM studies of elective EVAR versus OSR enrolling patients with intact AAA and reporting 5-year (at least) survival curves. Data regarding detailed inclusion criteria, duration of follow-up, and survival curves were abstracted from each individual study. In case of crossing of the combined survival curves, a pooled late-phase (between the crossing time and 5 years) hazard ratio (HR) for all-cause mortality was calculated.

Results: Our search identified 7 eligible studies (including 2 RCTs and 5 PSM studies) enrolling a total of 92,333 patients with AAA assigned to EVAR or OSR. Pooled survival rates after EVAR and OSR were 98.1% and 96.1 at 1 month, 94.2% and 93.1% at 1 year, 85.1% and 86.8% at 3 years, and 75.8% and 78.8% at 5 years, respectively. The survival curves crossed at 1.8 years with the survival rate of 90.5%. A pooled late-phase (between 1.8 years and 5 years) HR for calculated from data of the combined survival curves significantly favored OSR (1.29, 95% confidence interval, 1.24 to 1.35; $p < 0.00001$).

Conclusions: For intact AAA, although survival was better immediately after elective EVAR than OSR, the survival curves crossed at 1.8 years. Thereafter until 5 years, survival was worse after EVAR than OSR.

1. Introduction

In elective treatment for intact (non-ruptured) abdominal aortic aneurysm (AAA), endovascular aneurysm repair (EVAR) is associated with lower short-term all-cause mortality than open surgical repair (OSR) [1, 2]. This benefit from EVAR, however, does not persist at long-term follow-up [2–5]. Authors of previous meta-analyses of follow-up outcomes combined odds ratios (ORs) [2,4] or risk ratios (RRs) [3,5] for mortality. The most appropriate way of summarizing time-to-event (survival) data, however, is to use methods of survival analysis and express the intervention effect as a hazard ratio (HR) [6]. When comparing interventions in a study or meta-analysis a simplifying assumption is often made that the HR is constant across the follow-up period, even though hazards themselves may vary continuously, which is known as the proportional hazards assumption [6]. Our preliminary meta-analysis [7] pooling survival curves themselves of elective EVAR versus OSR for intact AAA, however, suggests that survival curves may cross; i.e. although EVAR yields better survival in the beginning of the study, this effect is reversed after some time. Under the proportional hazards assumption, crossing of the survival curves is impossible [8]. If the proportional hazards assumption fails to hold for the treatment, the HR cannot be interpreted as a relative risk [8]. In the present article updating our preliminary meta-analysis [7], to determine whether follow-up survival is better after elective EVAR than OSR for intact AAA, we combined 5-year survival curves themselves of EVAR and OSR in randomized controlled trials (RCTs) and propensity-score matched (PSM) studies. In case of crossing of the combined survival curves, a pooled late-phase (between the crossing time and 5 years) HR for all-cause mortality was calculated.

Abbreviations: AAA, abdominal aortic aneurysm; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR, endovascular aneurysm repair; HR, hazard ratio; IPD, individual patient data; OR, odds risk; OSR, open surgical repair; PSM, propensity-score matched; RCT, randomized controlled trial; RR, risk ratio.

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Abdominal Aortic Aneurysm Screening Reduces All-Cause Mortality: Make Screening Great Again

Hisato Takagi, MD, PhD[1], Tomo Ando, MD[2], Takuya Umemoto, MD, PhD[1]; for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

Abstract

We performed an updated meta-analysis of the longest (≥13 years) follow-up results from 4 randomized controlled trials of abdominal aortic aneurysm (AAA) screening in ≥64-year-old men. Invitation to screening reduced all-cause mortality significantly according to time-to-event data (hazard ratio: 0.98; 95% confidence interval [CI]: 0.96-0.99; $P = .003$) despite no reduction according to dichotomous data (odds ratio [OR]: 0.99; 95% CI: 0.96-1.01; $P = .23$). Invitation to screening reduced AAA-related mortality significantly (OR: 0.66; 95% CI: 0.47-0.93; $P = .02$) but did not reduce non-AAA-related mortality (OR: 1.00; 95% CI: 0.98-1.02; $P = .96$). All-cause, AAA-related, and non-AAA-related mortalities were significantly lower in attenders than in nonattenders, in noninvitees, or in both. All-cause (OR: 1.41; 95% CI: 1.23-1.63; $P < .00001$) and non-AAA-related mortalities (OR: 1.39; 95% CI: 1.18-1.64; $P < .0001$) were significantly higher in nonattenders than in noninvitees. In conclusion, invitation to AAA screening in ≥64-year-old men reduced both all-cause and AAA-related mortalities significantly. All-cause and non-AAA-related mortalities were significantly higher in nonattenders than in noninvitees, though both did not undergo screening.

Keywords

abdominal aortic aneurysm, meta-analysis, mortality, screening

Introduction

A systematic evidence review for the US Preventive Services Task Force[1] concluded that 1-time invitation for abdominal aortic aneurysm (AAA) screening in ≥65-year-old men was associated with decreased AAA rupture and AAA-related mortality but had little or no effect on all-cause mortality. The review[1] included 15-year results[2] of the Chichester trial, 13-year results[3] of the Multicentre Aneurysm Screening Study (MASS), 14-year results[4] of the Viborg Country trial, and 5-year results[5] of the Western Australia trial. However, our previous meta-analysis,[6] which included preliminary 11-year[7] instead of 5-year results[5] from the Western Australia trial, suggests that invitation to screening may reduce all-cause mortality. Recently, the Western Australia trial reported 13-year results[8] (never included in any published meta-analysis), in which there were no meaningful differences in all-cause, cardiovascular, and other mortalities. To determine whether invitation to AAA screening in men reduces mortality, we here performed an updated meta-analysis of the longest follow-up results from randomized controlled trials (RCTs).

Materials and Methods

Search Strategy

All RCTs of AAA screening in men were identified using a 2-level search strategy. First, databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through October 2016 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis. Search terms included *randomized*, *randomised*, or *randomly*; *abdominal aortic aneurysm/aneurysms*; and *screen*, *screened*, or *screening*.

Study Selection and Data Extraction

Studies considered for inclusion met the following criteria: the design was an RCT, the study population was men, participants were randomized to invitation versus no invitation to AAA screening, and outcomes included all-cause and AAA-related mortalities. Data regarding detailed inclusion criteria, duration

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Similar Survival After Repair vs Replacement for Ischemic Mitral Regurgitation

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To determine whether mitral valve (MV) repair improves early and late survival compared with MV replacement for patients with ischemic mitral regurgitation (IMR), we performed a meta-analysis of randomized controlled trials (RCTs) and adjusted observational studies. Databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through January 2016 using PubMed and Ovid. Studies considered for inclusion met the following criteria: the design was a RCT or adjusted observational study, the study population was patients with IMR; patients were assigned to MV repair vs replacement, and outcomes included early (30 days or in hospital) or late (≥1 year) overall survival or all-cause mortality. An adjusted odds or hazard ratio (OR/HR) with its 95% CI of early or late (including early) all-cause mortality for MV repair vs replacement was abstracted from each individual study. Our search identified 12 articles from one RCT and 10 adjusted observational studies including 2784 patients. Pooled analyses demonstrated no statistically significant difference in both early (OR = 0.90; 95% CI: 0.69-1.16; P = 0.41) and late mortality (HR = 0.90; 95% CI: 0.72-1.13; P = 0.38) between MV repair and replacement. Exclusion of any single study from the meta-analysis did not substantively alter the overall result of no statistically significant difference. There was no evidence of significant publication bias. For patients with IMR, MV repair appears to be unassociated with a significant decrease in both early and late all-cause mortality compared with MV replacement.

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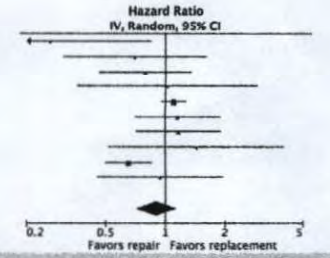

Forest plot of hazard ratios for late mortality after mitral repair vs replacement.

Central Message

MV repair, compared with replacement, for IMR is unassociated with a significant decrease in both early and late all-cause mortality.

Perspective Statement

We found that, based on a meta-analysis of one randomized controlled trial and 10 adjusted observational studies including 2784 patients with ischemic MR, MV repair is not likely to improve both early and late overall survival compared with MV replacement. Patients with IMR undergoing MV repair should be selected with caution being based on lack of its durability in correction of MR.

Recent meta-analyses combining observational studies of mitral valve (MV) surgery for patients with ischemic mitral regurgitation (IMR) suggest that MV repair may be associated with reduced early[1-5] and late[1,5] mortality compared with MV replacement. These meta-analyses pooled crude (ie, unadjusted) relative risk (RR) estimates abstracted from nonrandomized studies. Results should be always interpreted with caution, however, when they are included in meta-analyses because of greater potential biases for nonrandomized studies compared with randomized controlled trials (RCTs).[6] Particular concerns arise regarding differences between patients in different intervention groups (selection bias). Unlike for RCTs, it would usually be appropriate to analyze adjusted (rather than unadjusted) effect estimates, that is, analyses that attempt to control for confounding.[6] Furthermore, in only 1 (to our best knowledge) RCT, the Cardiothoracic Surgical Trials Network (CTSN) collaborators observed no significant difference in survival at 30 days,[7] 12 months,[7] and 2 years[8] between patients with IMR who underwent MV repair and those who underwent MV replacement. To determine whether MV repair improves early and late survival compared with MV replacement for patients with IMR, we performed a meta-analysis of RCTs and adjusted observational studies (with a propensity score, multivariate logistic regression, or multivariate Cox proportional hazards regression analysis).

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ORIGINAL ARTICLE

Association of chronic obstructive pulmonary, coronary artery, or peripheral artery disease with abdominal aortic aneurysm rupture

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ABSTRACT

BACKGROUND: Chronic obstructive pulmonary disease (COPD), coronary artery (CAD), and peripheral artery disease (PAD) are positively associated with abdominal aortic aneurysm (AAA) presence. It remains unclear, however, whether these 3 comorbidities are associated with AAA rupture. To assess the association of COPD, CAD, or PAD with AAA rupture, we reviewed currently available studies with a systematic literature search and meta-analytic estimates.

METHODS: Databases including MEDLINE and EMBASE were searched through December 2015 using PubMed and OVID. For each study, data regarding prevalence of COPD, CAD, or PAD in both the ruptured and non-ruptured groups were used to generate odds ratios (ORs) for rupture and 95% confidence intervals (CIs). Study-specific estimates were combined using inverse variance-weighted averages of logarithmic ORs in a random-effects model.

RESULTS: Our search identified 9 relevant studies including data on a total of 8873 AAA patients (rupture, 1241; non-rupture, 7632). Pooled analyses demonstrated that COPD was significantly and positively (OR, 1.51; 95% CI, 1.06 to 2.16; P=0.02), CAD was not significantly (OR, 0.83; 95% CI, 0.43 to 1.60; P=0.58), and PAD tended to be negatively (though non-significantly) associated with AAA rupture (OR, 0.44; 95% CI, 0.16 to 1.23; P=0.12).

CONCLUSIONS: Our analysis suggests that COPD is positively associated with AAA rupture, CAD is not associated with it, and PAD tends to be negatively associated with it. Further investigations would be required to understand precise mechanisms regarding the association of COPD, CAD, and PAD with AAA presence, growth, and rupture.

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Key words: Aortic aneurysm, abdominal - - Pulmonary disease, chronic obstructive - Coronary artery disease - Meta-analysis - Peripheral artery disease.

Since Cronenwett *et al.*[1] described in 1985 that degree of chronic obstructive pulmonary disease (COPD) was predictive of rupture of abdominal aortic aneurysm (AAA), it has been considered for 30 years that COPD may be positively associated with AAA rupture. The study by Cronenwett *et al.*,[1] however, included only 12 ruptured-AAA patients. In a recent large case-control study [2] consisting of 440 ruptured-AAA patients and 3605 non-ruptured-AAA patients, COPD prevalence was similar in the rupture and non-rupture groups (34% *versus* 37% in men; 43% *versus* 45% in women). Although the positive association of COPD with AAA presence is suggested in a recent meta-analysis,[3] no association of COPD with AAA growth is suggested in another recent meta-analysis.[4] Although coronary artery (CAD) and peripheral artery disease

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REVIEW
CARDIAC SECTION

Better midterm survival in women after transcatheter aortic valve implantation

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ABSTRACT

INTRODUCTION: In previous meta-analyses demonstrating better midterm overall survival in women undergoing transcatheter aortic valve implantation (TAVI), unadjusted risk and odds ratios were combined. To determine whether female gender is independently associated with better survival after TAVI, we performed a meta-analysis pooling adjusted hazard ratios (HRs) based on multivariate Cox proportional hazard regression.

EVIDENCE ACQUISITION: MEDLINE and EMBASE were searched through September 2015 using PubMed and OVID. Studies considered for inclusion met the following criteria: the study population was patients undergoing TAVI; and main outcomes included midterm (mean or median ≥6 months) overall survival or all-cause mortality in women and men. An unadjusted and/or adjusted HR of all-cause mortality for women *versus* men was abstracted from each individual study.

EVIDENCE SYNTHESIS: Of 1347 potentially relevant articles screened initially, 16 reports of eligible studies were identified and included. A primary meta-analysis of the 9 adjusted HRs demonstrated a significantly better midterm overall survival in women than men (N.=6891; HR=0.80; 95% confidence interval [CI]: 0.65 to 0.97; P=0.03). A secondary meta-analysis adding 5 statistically non-significant unadjusted HR also indicated better survival in women (N.=8645; HR=0.83; 95% CI: 0.72 to 0.96; P=0.01). Although statistical tests for the primary meta-analysis revealed funnel plot asymmetry in favor of women, the secondary meta-analysis produced a symmetrical funnel plot.

CONCLUSIONS: Female gender may be independently associated with better midterm overall survival after TAVI.

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Key words: Transcatheter aortic valve replacement - Survival - Women - Meta-analysis.

Introduction

Female gender is known to be a risk factor of postoperative mortality in cardiovascular surgery. Women undergoing isolated coronary artery bypass grafting (CABG) experience higher mortality at short-, mid-, and long-term follow-up compared with men.[1] They are older and have a higher prevalence of comorbidities including diabetes mellitus, hypertension, hyperlipidemia, peripheral vascular disease, and unstable angina.[1-4] The higher prevalence of these comorbid conditions is associated with higher risk for postoperative complications (including short-term mortality),[5, 6] which can also translate into increased incidence of cardiovascular events in the long term, resulting in higher mortality at 1 and 5 years.[2, 7, 8] Even in a sub-analysis of a meta-analysis [1] including propensity-score matched studies only, female gender remained significantly associated with higher short-term mortality after isolated CABG, which strengthens the evidence in favor of an association between female gender and post-CABG mortality. Additionally, women with abdominal aortic aneurysm (AAA) also have a higher mortality rate following elective open and endovascular repair.[9]

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REVIEW

Aortic diseases and obstructive sleep apnea

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ABSTRACT

INTRODUCTION: Obstructive sleep apnea (OSA), particularly moderate-to-severe OSA, increases all-cause mortality as well as cardiovascular events, and continuous positive airway pressure (CPAP) therapy can reduce cardiovascular events and mortality. In 2003, it was first shown that patients with thoracic aortic dissection (AD) presented a high prevalence of previously undiagnosed and frequently severe OSA. Since then, a number of authors have investigated the association of aortic diseases (including thoracic and abdominal aortic aneurysm as well as AD) with OSA.

EVIDENCE ACQUISITION: In the present article, we reviewed, with a systematic literature search through May 2015, currently available clinical studies investigating the association of aortic diseases with OSA.

EVIDENCE SYNTHESIS: It is suggested that OSA is highly prevalent in patients with aortic diseases and associated with aortic expansion. Through the nocturnal perturbations of intermittent hypoxia, intrathoracic pressure swings, and increased sympathetic neural activation, OSA patients appear to be at increased risk for vascular changes related to oxidative stress, inflammation, and endothelial dysfunction, which may present as risks for aortic diseases. Despite currently available findings, it remains unclear whether common etiology leads to both OSA and aortic diseases or whether OSA itself causes aortic diseases.

CONCLUSIONS: The following types of studies with long-term follow-up would be required: 1) a prospective cohort study comparing the incidence of aortic diseases in OSA patients with that in non-OSA subjects and 2) a randomized controlled trial determining whether CPAP therapy for OSA reduces the incidence of aortic diseases.

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Key words: Aortic aneurysm - Obstructive sleep apnea - Incidence.

Introduction

Several meta-analyses have recently confirmed that obstructive sleep apnea (OSA), particularly moderate-to-severe OSA, increases all-cause mortality as well as cardiovascular events [1-4] and further that continuous positive airway pressure (CPAP) therapy can reduce cardiovascular events and mortality.[2, 5] In 2003, Sampol *et al.*[6] first showed that patients with thoracic aortic dissection (AD) presented a high prevalence of previously undiagnosed and frequently severe OSA. Since then, a number of authors have investigated the association of aortic diseases (including thoracic [TAA] and abdominal aortic aneurysm [AAA] as well as AD) with OSA. In the present article, we reviewed, with a systematic literature search, currently available clinical studies investigating the association of aortic diseases with OSA.

Evidence acquisition

Databases including MEDLINE and EMBASE were searched through May 2015 using Web-based search engines (PubMed and OVID). Relevant studies were also identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were

Review

The association between body mass index and abdominal aortic aneurysm growth: a systematic review

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Summary: Diabetes, a state of relative insulin resistance, is negatively associated with both the presence and growth abdominal aortic aneurysms (AAA), which could suggest a protective role of obesity against AAA presence or growth. A recent meta-analysis demonstrated a trend toward a positive, though statistically non-significant, association between body mass index (BMI) and the presence of AAA. With respect to the association between obesity and AAA growth, however, the evidence had been very limited. To determine whether obesity (or BMI) is associated with AAA growth, we reviewed currently available studies with a systematic literature search. Our comprehensive search identified seven eligible studies reporting the association of BMI and AAA growth rates, which included data on a total of 3,768 AAA patients. All seven identified studies demonstrated no association between BMI and AAA growth. Despite a trend toward a positive association between BMI and AAA presence, the reason why BMI is not associated with AAA growth (suggested in the present review) is unclear. A discrepancy between associated comorbidities (coronary artery disease, peripheral artery disease, and chronic obstructive pulmonary disease) and AAA presence and between the same comorbidities and AAA growth, however, could be identified. Further investigations are required to elucidate why BMI is not associated with AAA growth despite the trend for a positive association with AAA presence.

Key words: Abdominal aortic aneurysm, body mass index, obesity, review

Introduction

Obesity is an established risk factor for cardiovascular disease. Although abdominal aortic aneurysms (AAA) share many risk factors with occlusive vascular disease, there are some distinct features of both diseases, such as the disparate association between diabetes with atherothrombosis and AAA [1, 2]. Type 2 diabetes, a state of relative insulin resistance, is *negatively* associated with both AAA *presence* [3, 4] and *growth* [5, 6]. These findings suggest a *protective* role of obesity against AAA *presence* or *growth* [1], because one of the main mechanisms by which obesity has been implicated in vascular disease is insulin resistance [7]. A recent systematic review of eight studies by Cronin et al. [1] suggests that anthropometric measures of body mass index (BMI) and waist circumference are associated with AAA *presence*. Our more recent meta-analysis [8] of 12 studies also demonstrated a trend toward a *positive*, though statistically non-significant, association between BMI and AAA *presence*. With respect to the association between obesity and AAA *growth*, however, the evidence had been very limited. A recent (published in 2013) systematic review [1] identified only two studies [9, 10] that investigated the association. To summarize the association between obesity (or BMI) and AAA *growth*, we reviewed currently available studies with a systematic literature search.

Methods

All studies reporting AAA growth rates were identified using a two-level search strategy. First, databases including MEDLINE and EMBASE were searched through July 2015 using web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual search of secondary sources including the references of the initially identified articles and a search of reviews and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analysis. Search terms included *enlargement*, *expansion*, *growth*, or *progression*; and *abdominal aortic aneurysm*.

Studies considered for inclusion met the following criteria: the design was unrestricted; the study population was AAA patients; and outcomes included data regarding the association of obesity (or BMI) with AAA growth rates. Two reviewers (authors) reviewed the eligible studies and determined whether they met the selection criteria. Data regarding detailed inclusion criteria, BMI, duration of follow-up, and AAA growth rates were abstracted (as available) from each individual study. Data were extracted in duplicate by two investigators (authors), and disagreements were resolved by consensus.

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Review

Associations of coronary and peripheral artery disease with presence, expansion, and rupture of abdominal aortic aneurysm – a grin without a cat!

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Summary: Both coronary and peripheral artery disease are representative atherosclerotic diseases, which are also known to be positively associated with presence of abdominal aortic aneurysm. It is still controversial, however, whether coronary and peripheral artery disease are positively associated with expansion and rupture as well as presence of abdominal aortic aneurysm. In the present article, we overviewed epidemiological evidence, i.e. meta-analyses, regarding the associations of coronary and peripheral artery disease with presence, expansion, and rupture of abdominal aortic aneurysm through a systematic literature search. Our exhaustive search identified seven meta-analyses, which suggest that both coronary and peripheral artery disease are positively associated with presence of abdominal aortic aneurysm, may be negatively associated with expansion of abdominal aortic aneurysm, and might be unassociated with rupture of abdominal aortic aneurysm.

Keywords: Abdominal aortic aneurysm, coronary artery disease, peripheral artery disease, review

Introduction

Both coronary and peripheral artery disease (CAD and PAD) are representative atherosclerotic diseases. These are also known to be *positively* associated with *presence* of abdominal aortic aneurysm (AAA) [1–4]. Namely, AAA prevalence/incidence is higher in patients with CAD than in subjects without CAD (in other words, CAD prevalence/incidence is higher in patients with AAA than in subjects without AAA) [1–4], and AAA prevalence/incidence is higher in patients with PAD than in subjects without PAD (in other words, PAD prevalence/incidence is higher in patients with AAA than in subjects without AAA) [1, 2]. It is still controversial, however, whether CAD and PAD are *positively* associated with *expansion* and *rupture* as well as with *presence* of AAA. In the present article, we overviewed epidemiological evidence, i.e. meta-analyses, regarding the associations of CAD and PAD with *presence*, *expansion*, and *rupture* of AAA through a systematic literature search.

Methods

All meta-analyses of the associations of CAD and PAD with *presence*, *expansion*, and *rupture* of AAA were identified. We searched MEDLINE and EMBASE databases until August 2016 using PubMed and OVID search engines. The following search terms were included: 1) *coronary (artery/arterial/heart) disease*, *ischemic/ischaemic coronary/heart disease*, *peripheral artery/arterial/vascular disease*, *claudication*, *claudicant*, or *ankle brachial index*; 2) *abdominal aortic aneurysm*; and 3) *meta-analysis*. Studies considered for inclusion met the following criteria: The design was a meta-analysis; studies which were included in a meta-analysis, investigated the associations of CAD and PAD with *presence*, *expansion*, and *rupture* of AAA.

The outcomes included the following pooled estimates: Relevant estimates included an odds ratio (OR)/hazard ratio (HR) for prevalence/incidence of AAA in patients with CAD (or PAD) versus subjects without CAD (or PAD), an OR/HR for prevalence/incidence of rupture in AAA patients with CAD (or PAD) versus those without CAD (or PAD), and mean difference (MD)/standardised MD (SMD) between expansion rates in AAA patients with CAD (or PAD) and those without CAD (or PAD).

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Association of Diabetes Mellitus With Presence, Expansion, and Rupture of Abdominal Aortic Aneurysm: *"Curiouser and Curiouser!" Cried Alice*

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ABSTRACT

Both coronary artery and peripheral artery disease are representative atherosclerotic diseases that are positively associated with presence of abdominal aortic aneurysm (AAA). Diabetes mellitus, which is one of major risk factors of coronary artery and peripheral artery diseases, however, has been curiously suggested to be negatively associated with AAA, despite the positive associations of coronary artery and peripheral artery diseases with presence of AAA. In the present article, we overviewed epidemiologic evidence (meta-analyses) regarding the associations of diabetes mellitus with presence, expansion, and rupture of AAA through a systematic literature search. Our exhaustive search identified seven meta-analyses. Main results of almost all meta-analyses (except for the two earliest ones) apparently found that diabetes mellitus is negatively associated with presence, expansion, and rupture of AAA.

1. Introduction

Both coronary artery disease and peripheral artery disease are representative atherosclerotic diseases that are positively associated with presence of abdominal aortic aneurysm (AAA) [1,2]. Diabetes mellitus (DM) is one of the major risk factors of coronary artery disease and peripheral artery disease, however, it has been curiously suggested to be negatively associated with AAA, despite the positive associations of coronary artery disease and peripheral artery disease with presence of AAA. In the present article, we overviewed epidemiologic evidence regarding the associations of DM with presence, expansion, and rupture of AAA through a systematic literature search. We searched MEDLINE and EMBASE databases until March 2016 using PubMed and OVID search engines. The following search terms were included: *diabetes*, *diabetic*, or *diabetics*; *abdominal*; *aorta* or *aortic*; *aneurysm* or *aneurysms*; and *meta-analysis*.

2. Association of DM with presence of AAA

DM may be negatively associated with presence of AAA (Table 1, Figure 1) [1,3–5], that is, prevalence or incidence of AAA may be lower in patients with DM than in subjects without DM, or prevalence/incidence of DM may be lower in patients with AAA than in subjects without AAA.

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Editorial

To complete, or not to complete, that is the question of revascularization in percutaneous coronary intervention with drug-eluting stents for multivessel disease

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In patients with multivessel (MV) coronary artery disease (CAD) (MV-CAD) except for acute myocardial infarction (acute MI, AMI) [including acute ST-segment elevation MI (STEMI)], the clinical impact of completeness of revascularization (RV) in percutaneous coronary intervention (PCI) with drug-eluting stents (DES) (DES-PCI) on major adverse cardiac (and cerebrovascular) events [MAC(C)E] remains unclear. Recently, Chang *et al.* (1) compared the outcomes in patients with MV-CAD achieving complete versus incomplete RV (C-RV *vs.* IC-RV) at the time of PCI. This analysis included consecutive 3,901 patients with MV-CAD undergoing DES-PCI, and the primary and secondary outcomes were all-cause death; and the rates of MI, stroke, and repeat RV (R-RV), respectively. Propensity-score matching was used, and 1,402 pairs of similar baseline characteristics in each group of C-RV and IC-RV were identified. As compared with C-RV at a median follow-up of 4.9 (interquartile range, 2.4 to 7.5) years, IC-RV was associated with similar risks of all-cause death [hazard ratio (HR), 1.03; 95% confidence interval (CI), 0.80 to 1.32; P=0.83], stroke (HR, 1.26; 95% CI, 0.76 to 2.09; P=0.37), and R-RV (HR, 1.15; 95% CI, 0.93 to 1.41; P=0.19); but a higher risk of MI (HR, 1.86; 95% CI, 1.08 to 3.19; P=0.024). As compared with C-RV in patients with MV-CAD (except for STEMI) treated with DES-PCI, the authors (1) concluded that IC-RV was associated with a similar risk of all-cause death but a higher risk of MI during follow-up.

A number of meta-analyses (2-4) have been performed to focus C-RV versus IC-RV in PCI or coronary artery bypass grafting (CABG) in patients with MVD (except for AMI). In unrestricted PCI, the first meta-analysis by Garcia *et al.* (2) of 35 studies including 89,883 patients with 4.6±4 years follow-up showed that C-RV was associated with lower all-cause death [risk ratio (RR), 0.73; 95% CI, 0.65 to 0.82; P<0.001], MI (RR, 0.80; 95% CI, 0.71 to 0.91; P=0.001), and R-RV (RR, 0.72; 95% CI, 0.63 to 0.81; P<0.001) relative to IC-R. In unlimited CABG, however, C-RV was associated with lower all-cause death (RR 0.70; 95% CI, 0.62 to 0.80; P<0.001); but with neither MI (RR, 0.69, 95% CI, 0.44 to 1.10; P=0.12) nor R-RV (RR, 0.92; 95% CI, 0.67 to 1.28; P=0.64) (2). In PCI with stents (including not only DES but also bare-metal stents), a recent meta-analysis by Zimarino *et al.* (3) of 28 studies including 83,695 patients with 4.7±4.3 years follow-up confirmed that C-RV conferred clinical benefits in all-cause death (RR, 0.73; 95% CI, 0.64 to 0.82), MI (RR, 0.69; 95% CI, 0.59 to 0.82), and R-RV (RR, 0.74; 95% CI, 0.63 to 0.86) as compared with IC-R. In CABG with arterial graft(s) in ≥80% of cases, however, C-RV was associated with reduced all-cause death (RR, 0.76; 95% CI, 0.63 to 0.90); but with neither MI (RR, 0.89; 95% CI, 0.67 to 1.18) nor R-RV (RR, 0.94; 95% CI, 0.65 to 1.36) (3). Another recent meta-analysis (4) of exclusive adjusted-risk estimates from 14 studies enrolling 30,389 patients demonstrated a statistically significant reduction in follow-up mortality with C-RV relative to IC-RV CABG (HR, 0.63; 95% CI, 0.53 to 0.75;

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Letter to the Editor

Aliceology: Alice in literature-land

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To the Editor:

"Alice's Adventure in Wonderland" and "Through the Looking-glass, and What Alice Found There" written by Lewis Carroll were published in 1865 and 1871, respectively. Ever since Clark [1] first used "Alice in Virusland" as a title in 1938, the term of "Alice" paying homage to Carroll's novels has been widely appearing in the literature for nearly 80 years. To examine the so-called "aliceology," i.e. how researchers use the term of "Alice" in medical literature contemporarily, I reviewed the title of articles published in the 21st century.

MEDLINE database was searched using PubMed from January 2001 to August 2015. Of 166 potentially relevant articles screened initially, 133 were excluded (proper noun, 95; Alice in wonderland syndrome, 29; letter, 5; duplication, 3; retraction, 1) and the remaining 33 articles were reviewed.

"Alice in wonderland" related titles were identified in 20 articles (60.6%), use as an acronym in 4, "Alice" only use in 3, "Down the rabbit hole" (title of the novel's first chapter) related titles in 2, "'Curiouser and curiouser!' cried Alice" in one, "Alice through the looking glass" in one, and mention for the novel itself in 2. In the articles with the "Alice" only use, "Alice" is "a patient with advanced non-small cell lung cancer who struggles with taxane-related peripheral neuropathy," "a woman of less-than-average height, who if she is both sensible and lucky is a never-smoker, drinks alcohol only in moderation, and is able to maintain a healthy weight through diet and exercise," or "a watchful invisible person." In addition to "Alice 'in wonderland'" used the most commonly; "in lipidland," "in meta-analysis," "'still' in the Wonderland," "in actuarial-land," "in radiation protection land," "in migraineland," "in menopauseland," "in healthcare wonderland," and "in caspase land" were used as metaphor of an intricate and controversial field of research.

The tone of the novel "Alice's Adventure in Wonderland" may be light and playful, and the author's intent to entertain, but there can be no doubt that the novel also succeeds as a vivid demonstration of human psychopathology — albeit mostly in animals [2]. Alice experiences a worrying array of visual distortions and disturbances, as she reports her overall size to be increasing and decreasing on several occasions. Alice also exhibits worrying disturbances of core self-identity, leading to a fluid, inconsistent sense of self and a constant feeling of uncertainty about who she really is [2]. Hazelton and Hickey [3] suggest in their article titled "Cinderology" that the identification of a particular disease or mechanism as a "Cinderella," a neglected young woman who later receives widespread recognition and admiration, may reflect the author's protective affection for his or her area of study. That is, lonely researchers slaving away at their bench, studying an obscure medical phenomenon of interest to no one but themselves, may well imagine the day when *Cinderella meets Prince Serendip* [4], a legendary ruler of Ceylon who renowned for his happy knack of chance discovery [3]. The intricate and controversial field of research where the author is struggling may be reflected in a particular area of study identified as a "Wonderland" into which Alice strayed. Alice's sister pictured to herself how Alice would gather about her other little many children, and make their eyes bright and eager with many a strange tale, perhaps even with the dream of "Wonderland." In the same way as the tale of Alice has been captivating children all over the world, authors may fantasize about being invited to present at an important conference where they might enthrall a large audience with the fruits of their labor in "Wonderland."

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Reply to the letter to the editor: Make surgery proud again

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We would like to greatly acknowledge the comments by Paraskevas on our article [1] recently published in International Journal of Cardiology. Since 2005, we have published a number of articles [Supplemental References S1–S9] on the topic of elective endovascular aneurysm repair (EVAR) versus opens surgical repair (OSR) for intact abdominal aortic aneurysm, which includes the article [S7] cited by Paraskevas. These article, as well as other meta-analyses and systematic reviews, assessed "entire" (from the intervention to the last follow-up) survival. The last [S9] and present meta-analyses [1] of ours pooling survival curves themselves, however, demonstrated that survival curves after EVAR and OSR cross: i.e. although EVAR yields better survival in the beginning of the study, this effect is reversed after some time. Crossing of the survival curves is impossible under the proportional hazards assumption, and the hazard ratio (HR) cannot be interpreted as a relative risk if the proportional hazards assumption fails to hold for the treatment [2]. Thus, we assessed the "late-phase" HR only after the crossing time of the pooled survival curves, not the "entire" HR both before and after the crossing time [1]. The survival rate (90.5%) after EVAR is equal to that after OSR at the crossing time of 1.8 years (though, before the crossing time, survival is better after EAVR than after OSR), and the pooled "late-phase" (after the crossing time: i.e. between 1.8 years and 5 years) HR demonstrates significantly worse survival after EAVR than after OSR (1.29; 95% confidence interval [CI], 1.24 to 1.35; $p < 0.00001$), both of which suggest that, at 5 years, the survival rate is significantly worse after EVAR (75.8%) than after OSR (78.8%) even though the inappropriate (because of crossing of the survival curves) pooled "entire" (before and after the crossing time: i.e. between the intervention and 5 years) HR indicated no significant difference in survival between OSR and EAVR. Most recently, the EVAR trial (ISRCTN55703451) investigators [3] also showed that patients in the EVAR group had significantly lower mortality at 0 to 6 months after randomization ("early-phase" HR, 0.61; 95% CI, 0.37 to 1.02; $p = 0.14$) but those in the OSR group had significantly lower mortality beyond 8 years of follow-up ("late-phase" HR, 1.25; 95% CI, 1.00 to 1.56, $p = 0.048$), despite no significant difference in mortality over the course of follow-up between the EVAR and OSR groups ("entire" HR, 1.11; 95% CI, 0.97 to 1.27; $p = 0.14$), which strengthens our assessment of the "late-phase only" HR. We would like to make OSR proud again.

Second, the comment by Paraskevas regarding a subgroup meta-analysis by gender must be very important. Regrettably, however, none of 7 reports [S10–S16] included in the present meta-analysis [1] of ours provided gender-stratified mortality. Further investigation on this issue would be required.

Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2017.02.037.

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ACQUIRED CARDIOVASCULAR DISEASE
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Percutaneous versus surgical cut-down access in transfemoral transcatheter aortic valve replacement: A meta-analysis

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Abstract

BACKGROUND: The transfemoral (TF) approach has become the preferred approach for transcatheter aortic valve replacement (TAVR) because of its low risk profile. However, the relative safety of the percutaneous approach (PC) compared to surgical cut-down (SC) remains unclear. Our aim was to compare the outcomes between PC versus SC access in patients undergoing TF-TAVR using a meta-analysis.

METHODS: We conducted a systematic electronic database search for studies reporting major and minor vascular complications (VC), major and minor bleeding, and perioperative all-cause mortality, in PC versus SC TF-TAVR cases. Complications were reported based on the Valve Academic Research Consortium criteria. A random-effects model was used to calculate odds ratios and 95% confidence intervals.

RESULTS: Eight observational cohort studies and one randomized control trial (2513 patients in PC and 1767 patients in SC) were included in the analysis. Major and minor VC, as well as bleeding complications, were comparable between the two approaches. The need for surgical intervention for VC was comparable between PC and SC. There was no difference in perioperative all-cause mortality.

CONCLUSIONS: PC and SC have similar safety profiles and outcomes when used appropriately in selected patients.

1 | INTRODUCTION

The optimal method of performing vascular access for transfemoral (TF) transcatheter aortic valve replacement (TAVR)—percutaneous access (PC) versus surgical cut-down (SC)—remains controversial. Both approaches possess unique advantages. PC is less invasive and faster, while SC provides excellent vascular control and the ability to repair a damaged vessel. While previous studies have shown the feasibility and safety of PC and SC, it remains unclear which approach offers the better safety profile.[1–3] Despite the advancement in technologies, TF-TAVR remains associated with vascular complication rates of 2–20%.[4] SC is still performed at many centers. According to one of the largest TAVR registries including >20,000 patients and across more than 300 centers, PC and SC were utilized in 58.7% and 41.3% in TF-TAVR.[5] We sought to compare the perioperative complications and outcomes in PC TF-TAVR and SC TF-TAVR using a systematic review and meta-analysis.

2 | METHODS

The systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines.[6,7]

A systematic search of medical literature databases PUBMED and EMBASE was conducted for observational cohort studies and randomized clinical trials (RCTs). The search date was limited from January 1st, 2002 to June 13th, 2016. Search terms were (transcatheter aortic valve implantation, TAVR, transcutaneous aortic valve replacement, tavi, tavr, sapien, corevalve) AND (vascular, access, cut down). There were no language limitations. Conference abstracts were excluded. Selected manuscripts were screened by two independent reviewers (T.A. and A.B.) based on titles and/or abstracts and when considered relevant, included for full manuscript review based on inclusion and exclusion criteria. Reference lists of those

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Sapien 3 versus Sapien XT prosthetic valves in transcatheter aortic valve implantation: A meta-analysis

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ABSTRACT

Objectives: The S3 prosthetic valve was introduced to overcome several issues with its predecessor, the SXT, in transcatheter aortic valve implantation (TAVI), however, the clinical outcomes of this new model are not clearly defined. We performed a meta-analysis to compare the outcomes in Sapien 3 (S3) and Sapien XT (SXT) recipients.
Methods: A literature search through PUBMED and EMBASE was conducted. Articles that included at least one of the clinical outcomes of interest were included in the meta-analysis: moderate to severe paravalvular regurgitation (PVR), permanent pacemaker implantation (PPI), major vascular complications (MVC), cerebrovascular events (stroke and transient ischemic attack) (CVE), failure rate of device implantation, life-threatening, disabling or major bleeding, need for post-dilation and early all-cause-mortality.
Results: A total of 9 observational cohort studies were included. S3 was implanted in 945 and SXT in 1553 patients. S3 was associated with a lower incidence of moderate to severe PVR (1.6% vs 6.9%, $p < 0.0001$), lower MVC (5.1% vs 8.9%, $p = 0.01$) and less serious bleeding (8.1% vs 15.2%, $p = 0.003$) compared to the SXT. Device deployment failure rate was lower in the S3 (1.2% vs 5.9%, $p = 0.004$) and the S3 required less post-dilation (16.9% vs 26.9%, $p = 0.05$). Rates of CVE, perioperative mortality and PPI were similar between the two valves.
Conclusions: Implantation of the S3 prosthetic valve results in lower rates of moderate to severe PVR, MVC, post-dilation and serious bleeding however it does not improve on the SXT in terms of CVE, PPI and early mortality.

1. Introduction

Prosthetic heart valve technology and operator technique utilized in transcatheter aortic valve implantation (TAVI) have successfully achieved similar long-term survival rates compared to traditional surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis (AS). However, TAVI has not yet proven long-term superiority over SAVR in terms of other secondary outcomes [1,2]. Rates of paravalvular regurgitation (PVR) and major vascular complications (MVC) remain high and add significant morbidity to TAVI recipients. [3,4]. The Sapien XT (SXT: Edwards Lifesciences, Irvine, California) prosthetic heart valve received FDA approval in June 2014 to overcome limitations of the original Sapien valve. However, it failed to demonstrate improved outcomes compared to its predecessor. Webb et al. reported similar rates of major or disabling bleeding, pacemaker implantation rate and stroke. Vascular complications decreased but moderate PVR was higher in SXT at 30 days and unchanged at one year. In addition, mild and severe PVR was unchanged. Most importantly, 30 day and one year all-cause and cardiovascular mortality were similar [5]. Although SXT decreased vascular complications, it failed to reduce many other perioperative complications. Therefore, it became imperative to pursue a newer generation of prosthetic valve to overcome these issues. This led to the advent of the Sapien 3 valve (S3: Edwards Lifesciences Inc., Irvine, CA, USA), which was designed specifically to address perioperative complications like PVR and MVC by outer skirt sealing and smaller sheath profile. The S3 valve received approval for use in Europe and the United States in January 2014 and June 2015, respectively. So far clinical outcomes appear promising in single-arm studies [6,7]. Several studies have compared the outcomes of the S3 to the SXT [8–13], however, these studies have been limited in size. It is paramount to determine the outcomes of this newer generation of balloon-expandable prosthetic valve compared to the previous generation. Therefore, we sought to investigate the performance of the S3 compared to the SXT through systematic review and meta-analysis.

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Review

The Prognostic Impact of New-Onset Persistent Left Bundle Branch Block Following Transcatheter Aortic Valve Implantation: A Meta-analysis

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ABSTRACT

New-onset persistent left bundle branch block (NOP-LBBB) is one of the most common conduction disturbances after transcatheter aortic valve implantation (TAVI). We hypothesized that NOP-LBBB may have a clinically negative impact after TAVI. To find out, we conducted a systematic literature search of the MEDLINE/PubMed and Embase databases. Observational studies that reported clinical outcomes of NOP-LBBB patients after TAVI were included. The random-effects model was used to combine odds ratios, risk ratios, or hazard ratios (HRs) with 95% confidence intervals. Adjusted HRs were utilized over unadjusted HRs or risk ratios when available. A total of 4049 patients (807 and 3242 patients with and without NOP-LBBB, respectively) were included. Perioperative (in-hospital or 30-day) and midterm all-cause mortality and midterm cardiovascular mortality were comparable between the groups. The NOP-LBBB patients experienced a higher rate of permanent pacemaker implantation (HR: 2.09, 95% confidence interval: 1.12-3.90, $P = 0.021$, $I^2 = 83\%$) during midterm follow-up. We found that NOP-LBBB after TAVI resulted in higher permanent pacemaker implantation but did not negatively affect the midterm prognosis. Therefore, careful observation during the follow-up is required.

Introduction

Transcatheter aortic valve implantation (TAVI) has shown a comparable long-term prognostic benefit compared with surgical aortic valve replacement (SAVR) for severe symptomatic aortic stenosis in both high and intermediate surgical risk.[1,2] However, several perioperative complications may diminish the benefit of TAVI and be observed more frequently than following SAVR. New-onset persistent left bundle branch block (NOP-LBBB) is one of the most frequent conduction disturbances observed following TAVI and could potentially attenuate the benefit of the procedure.[3,4]

Left bundle branch block causes electrical and mechanical dyssynchrony of the heart and various unfavorable hemodynamic effects.[5] Previous studies have reported its negative prognostic impact on wide variety of cardiac disorders.[6–8] Hoffman et al have reported that new-onset LBBB or permanent pacemaker implantation (PPI) following TAVI was an independent risk factor for reduced left ventricular ejection fraction (LVEF) at 12-month follow-up.[9] More importantly, according to Urena et al, NOP-LBBB is associated with increased sudden cardiac death following TAVI.[10] However, the prognostic impact of NOP-LBBB following TAVI has not yet been established. Schymik et al have reported NOP-LBBB as an independent risk factor for all-cause mortality, but other studies have not found an association between NOP-LBBB and all-cause mortality.[11–13] Because new-onset LBBB is a rare conduction disturbance with no clear association with mortality following SAVR, it is paramount to assess the prognostic impact of NOP-LBBB following TAVI to improve its outcomes.[14]

Therefore, we sought to summarize the prognostic impact of NOP-LBBB following TAVI through a meta-analysis.

Methods

Search Strategy

A systematic literature search was conducted through February 2016. We set neither time nor language restrictions. Two independent reviewers (T.A. and H.T.) searched the MEDLINE/PubMed and Embase databases. Search terms: (1) "left bundle branch block" or "LBBB" or "conduction"; and (2) "transcatheter aortic valve" or "percutaneous aortic valve" or "TAVI" or "TAVR" or "transfemoral" or "transapical" or "transsubclavian" or "transaortic" or "transcarotid" or "Sapien" or "CoreValve" or "balloon expandable" or "self expandable." We utilized a

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Article in Press

Trends in Vascular Complications in High Risk Patients Following Transcatheter Aortic Valve Replacement in the United States

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Vascular complications (VC) following transcatheter aortic valve replacement (TAVR) is associated with worse outcomes. The trend of VC incidence in patients considered high-risk is unclear. We sought to assess the trend of VC after TAVR in patients at high-risk. We investigated the VC trend in female, diabetes (DM) and peripheral vascular disease (PVD). Patients who underwent TAVR from 2011 to 2014 in the United States were identified using ICD-9 code 35.05 from the Nationwide Inpatient Sample database. Frequency of any VC (per 100 TAVI procedure or hospital discharges) for each year from 2011 through 2014 was assessed for the overall population as well as within each category of high-risk cohorts. The overall VC rate was 6.0% (2,044/33,790). Patients who had VC were more likely to be female and had higher rates of PVD at baseline. The annual rate of VC in the overall population from 2011 to 2014 was 4.6%, 9.4%, 6.8% and 4.4%, respectively. There was a significant increase in VC rate from 2011 to 2012 ($p=0.03$) whereas there was a significant decrease in VC rate from 2012 to 2014 ($p<0.001$). The rate of VC between 2011 and 2014 were similar ($p=0.82$). The rate of VC did not increase in any of the high-risk groups from 2011 to 2012. However, the rate of VC from 2012 to 2014 decreased significantly in all of the high-risk groups. The VC rate was similar for groups between 2011 and 2014. The overall VC rate among TAVR patients initially increased from 2011 to 2012 but decreased thereafter. Similar trend in VC rate was found among high-risk patients except that the initial increase in rates from 2011 to 2012 did not reach statistical significance. Whether further reduction in VC with improvement in devices and operator/center experience for both overall and high-risk groups in TAVR occurs will require continuous longitudinal monitoring.

Key word:
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Original Article

Comparison of late mortality after transcatheter aortic valve implantation versus surgical aortic valve replacement: Insights from a meta-analysis

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ABSTRACT

Introduction: Transcatheter aortic valve implantation (TAVI) has shown non-inferior late mortality in severe aortic stenosis (AS) patients in intermediate to inoperable risk for surgery compared to surgical aortic valve replacement (SAVR). Late outcome of TAVI compared to SAVR is crucial as the number of TAVI continues to increase over the last few years.

Methods: A comprehensive literature search of PUBMED and EMBASE were conducted. Inclusion criteria were that [1] study design was a randomized controlled trial (RCT) or a propensity-score matched (PSM) study: [2] outcomes included >2-year all-cause mortality in both TAVI and SAVR. The random-effects model was utilized to calculate an overall effect size of TAVI compared to SAVR in all-cause mortality. Publication bias was assessed quantitatively with Egger's test.

Results: A total of 14 studies with 6503 (3292 TAVI and 3211 SAVR, respectively) were included in the meta-analysis. There was no difference in late all-cause mortality between TAVI and SAVR (HR 1.17, 95%CI 0.98–1.41, $p = 0.08$, $I^2 = 61\%$). The sub-group analysis of all-cause mortality of RCT (HR 0.93 95%CI 0.78–1.10, $p = 0.38$, $I^2 = 40\%$) and PSM studies (HR 1.44 95%CI 1.15–1.80, $p = 0.02$, $I^2 = 35\%$) differed significantly (p for sub-group differences = 0.002). Meta-regression implicated that increased age and co-existing CAD may be associated with more advantageous effects of TAVI relative to SAVR on reducing late mortality. There was no evidence of significant publication bias ($p = 0.19$ for Egger's test).

Conclusions: TAVI conferred similar late all-cause mortality compared to SAVR in a meta-analysis of RCT but had worse outcomes in a meta-analysis of PSM.

1. Introduction

Since the successful first in man case of transcatheter aortic valve implantation (TAVI) in a patient with inoperable, symptomatic severe aortic stenosis (AS) in 2002 by Cribier et al., the number of TAVI performed worldwide has been dramatically increasing [1–3]. TAVI has shown promising result not only for severe AS patients in high operative risk but also in intermediate surgical risk [4–6].

Patients at intermediate risk are expected to have the longer life expectancy after TAVI compared to those at high or inoperable risk. The data on late outcomes after TAVI is starting to accumulate. Several studies have reported 3 to 7 years of outcome data after TAVI [7–13]. However, a number of studies that have reported comparative late outcomes between TAVI and surgical aortic valve replacement (SAVR) are relatively limited. The United States CoreValve Registry showed all-cause mortality favoring TAVI ($p = 0.068$) during 3 years follow-up, while the Placement of AorRTic TraNscathetER (PARTNER) valve trial have reported similar 5 years all-cause mortality [14,15].

Recently, a meta-analysis of long-term outcomes (>1 year) between TAVI and SAVR has been reported using odds ratio (OR) [16]. However, an estimate of late outcome is better assessed with hazards ratio (HR) than OR [17]. Recent other meta-analyses showed improved mortality in TAVI than SAVR during up to 2 years or median of 2 (range 3 months to 3 years) years follow-up with limited number of studies [18,19]. We have previously published meta-analysis of TAVI vs SAVR using propensity-score analysis and concluded that TAVI had worse outcome compared to SAVR [20]. In the same report, meta-analysis of 4 randomized clinical trials (RCT) [15,21–23] was performed. However, our previous report included in that studies, approximately half (10 studies) had follow-up duration <2 years [20]. In addition, out of the 4 RCTs included only two had follow-up >2 years [15,22]. It is of great

Abbreviations: AS, aortic stenosis; CAD, coronary artery disease; HR, hazards ratio; NOTION, Nordic Aortic Valve Intervention; OR, odds ratio; PARTNER, Placement of AorRTic TraNscathetER; PSM, propensity-matched; RCT, randomized control trial; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

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0953-6205/

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Comparison of Hospital Outcome of Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Diabetes Mellitus (from the Nationwide Inpatient Sample)

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The comparative outcomes of transcatheter aortic valve replacement (TAVR) versus surgical aortic valve replacement (SAVR) in diabetes mellitus (DM) patients are scarce. We aimed to assess and compare the outcomes of TAVR versus SAVR in DM patients using the Nationwide Inpatient Sample database from 2011 to 2013. A complete case analysis was performed for the multivariate analysis and cases with missing data were excluded. The primary end point was in-patient all-cause mortality and secondary outcomes were perioperative complications. An estimated 5,719 TAVR procedures and 65,096 SAVR procedures were performed among DM patients in the United States between 2011 and 2013. TAVR patients were older (80 ± 8.1 vs 70 ± 10, p <0.001), majority of them were women (45% vs 38%, p <0.001), and predominantly white race (total of 80%). The adjusted odds ratio (OR) for the primary outcome was significantly lower in TAVR patients (2.8% vs 3.6%, OR 0.63, p = 0.02). TAVR patients were also at lower risk for bleeding requiring transfusions (13% vs 20%, OR 0.43, p <0.01), cardiac complications (6.1% vs 14%, OR 0.34, p <0.01), respiratory complications (1.2% vs 3.7%, OR 0.26, p <0.01), postoperative sepsis (1.7% vs 3.6%, OR 0.45, p = 0.03), and acute myocardial infarction (2.5% vs 2.9%, OR 0.62, p <0.01), compared with SAVR patients. Conversely, TAVR patients were at increased risk for vascular complications (5.7% vs 3.9%, OR 1.5, p <0.01) and new pacemaker implantation (10% vs 5.7%, OR 1.5, p <0.01). The mean hospitalization cost was lower for TAVR than SAVR ($58,878 vs $63,869, p = 0.003). Length of stay (median 6 vs 8 days, p <0.001) was shorter in TAVR patients. In conclusion, TAVR may result in better in-hospital outcome than SAVR in DM patients. © 2017 Elsevier Inc. All rights reserved. **(Am J Cardiol 2017;■:■−■)**

Diabetes mellitus (DM) is associated with worse outcomes in both transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).[1–3] However, few studies have compared outcomes of TAVR versus SAVR in DM patients. Lindman et al[4] reported tendency toward better 30-day outcomes between transfemoral-TAVR and SAVR in DM patients. However, this is a post hoc analysis from the Placement of Aortic Transcatheter Valve (PARTNER) trial. To further assess the clinical outcomes of TAVR versus SAVR in DM patients using the "real-world" practice database would provide clinicians and patients with useful information in determining the optimal treatment strategy for patients with severe symptomatic aortic stenosis. Therefore, we compared the in-hospital outcomes in TAVR and SAVR using the Nationwide Inpatient Sample (NIS) database.

Methods

This study was conducted using the NIS database of the Health Care Utilization Project. Details of the design and description of the NIS database is available online (*https://www.hcup-us.ahrq.gov/*). Briefly, NIS is the largest nationally representative database of all hospital discharges in the United States from 1998. It is a 20% stratified sampling of discharges from US community hospitals, excluding rehabilitation and long-term acute care hospitals. Each year, over 7 million hospital stays are sampled nationwide, which, when weighted, estimates more than 35 million hospitalizations annually.

This study utilizes information on DM patients (age ≥ 18 years) who underwent SAVR or transfemoral/transaortic TAVR in the United States between 2011 and 2013. SAVR cases were identified using International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes 35.21 and 35.22, whereas TAVR cases were identified by ICD-9 procedure code 35.05.

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See page 3 for disclosure information.

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Reviews

Percutaneous Closure of Paravalvular Regurgitation After Transcatheter Aortic Valve Implantation: A Systematic Review

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ABSTRACT

Paravalvular regurgitation (PVR) remains one of the drawbacks of transcatheter aortic valve implantation (TAVI). Details of percutaneous closure (PCC) of PVR after TAVI remain obscure. We aimed to explore the patient characteristics, procedural details, closure devices used, and outcomes of PCC after TAVI. A systematic search of the MEDLINE/PubMed and Embase databases from January 2002 to September 2015 was conducted. Reports considered to include same patient were excluded and only the studies with largest cohorts were included. A total of 14 studies including 58 patients (61 cases) were included in the study. A balloon-expandable (BE) valve was used more frequently compared with a self-expandable (SE) valve (72.6% vs 27.4%, respectively). The mean success rate was 86.9% (100% and 77.8%, respectively; $P = 0.097$). The median number of closure devices used was 1 (range, 1–4) and did not differ between SE and BE valves ($P = 0.71$). Mean time from index procedure to PCC did not differ between SE and BE valves (295 ± 380 days vs 379 ± 353 days; $P = 0.71$). Seven patients had history of valve-in-valve and 6 patients had procedural success. Among the patients with available follow-up data (94.8%), there were 15 deaths (27.3%). Percutaneous closure of PVR after TAVI had a high success rate in selected patients in both BE and SE valves. The success rate, timing, and number of closure devices were similar between BE and SE valves. However, prognosis remains fairly poor.

Introduction

Paravalvular regurgitation (PVR) is one of the main drawbacks of transcatheter aortic valve implantation (TAVI) as compared with surgical aortic valve replacement (SAVR). Previous articles have reported its negative prognostic impact following TAVI in both midterm and long-term follow-up.[1,2] Some reports suggest that even mild PVR could affect the prognosis.[3] Even though the second-generation TAVI prosthetic valves are promising in decreasing the PVR rate, their long-term valve durability has not yet been proven.[4]

Revision cardiac surgery in TAVI patients is less desirable, as these patients were deemed high or inoperable surgical risks prior to TAVI. Postdilation (PD) and valve-in-valve (ViV) have been widely performed for the treatment of PVR after TAVI. However, the treatment strategy for PVR after TAVI is not standardized, and it remains largely dependent on institutions and operators. In addition, these 2 commonly utilized treatment modalities are not free from complications.[5,6]

Percutaneous closure (PCC), although it appears to be an attractive additional treatment option, has not been studied in detail compared with the aforementioned 2 treatment modalities. Past reports have been restricted only to case reports and case series with small numbers of patients.[7,8] Concerns regarding its technical difficulty and safety could be one of the reasons for underutilization of this method.

Therefore, we aimed to systematically review the current published articles to elucidate patient characteristics, procedural details, closure devices used, and outcomes in PCC after TAVI.

Methods

Search Strategy

A systematic literature search was conducted through MEDLINE/PubMed and Embase databases from January 1, 2002, to March 17, 2016. Observational studies and case series/reports were searched with the following search terms: (1) "TAVI" or "TAVR" or "transcatheter aortic valve replacement" or "transcatheter aortic valve implantation" or "CoreValve" or "Sapien" or "balloon expandable" or "self expandable"; and (2) "closure" or "paravalvular" or "perivalvular" or "periprosthetic" or "paraprosthetic."

Abstracts/titles were screened for relevant articles, and if they were considered to include information related

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Additional Supporting Information may be found in the online version of this article.

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健常者におけるRhoキナーゼ阻害薬リパスジル塩酸塩水和物による視神経乳頭血流への影響

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Influence of Rho Kinase Inhibitor Ripasudil Instillation on Optic Nerve Head Blood Flow in Healthy Volunteers

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目的：健常者におけるリパスジル塩酸塩水和物点眼による視神経乳頭血流の変化を検討する．**対象および方法**：屈折異常以外の眼疾患を有しない健常者12例を対象とし，0.4%トロピカミドによる散瞳後，片眼にリパスジル点眼を，他眼に生理食塩水を点眼し，1，2，4，6時間後に体血圧，脈拍数，両眼圧および視神経乳頭血流の変化率（mean blur rate：MBR）をレーザースペックル法で測定した．MBRは，上方，下方，耳側，鼻側の4つの区域に分け，各領域の組織MBR（mean of tissue area：MT），血管MBR（mean MBR in vessel area：MV），全領域MBR（mean of all area：MA）として測定し比較検討した．**結果**：視神経乳頭全体では，点眼6時間後のMTが点眼前と比べ有意に増加していた．耳側では，4時間後のMA，MTと，6時間後のMT，MVが点眼前と比べ有意に増加した．眼圧は対照側と比べ有意に低下した．全身血圧と脈拍数は開始前と比べ有意な変化はなかった．**結論**：健常者においてリパスジル点眼は眼圧下降のみならず視神経乳頭血流を増加させることが示された．

Purpose：To examine whether the rho kinase inhibitor ripasudil influences optic nerve head (ONH) blood flow in healthy volunteers. **Patients and methods**：Subjects comprised 12 healthy volunteers. Mean blur rate (MBR) was measured by laser speckle method on ONH and in each of 4 sectors (superior, temporal, inferior, nasal), before and at 1, 2, 4 and 6 hours after ripasudil instillation in one eye and saline in the fellow eye. Systemic blood pressure (SBP), pulse rate (PR) and intraocular pressure (IOP) were measured at each instillation. **Results**：There were no significant changes in SBP or PR. IOP showed a significant decrease at 1 hour compared to that before instillation, and lower levels were maintained. The change rate significantly increased for MT on the entire ONH at 6 hours, MA/MT at 4 hours and MT/MV at 6 hours on the temporal sector after ripasudil instillation. **Conclusion**：Ripasudil increases ONH blood flow and is considered to be a neuroprotective drug.

〔Atarashii Ganka (Journal of the Eye) **33**(8)：1226～1230，2016〕

Key words：Rhoキナーゼ阻害薬，リパスジル，視神経乳頭血流，レーザースペックル．Rho kinase inhibitor, ripasudil, optic nerve blood flow, laser speckle.

はじめに

ROCK（Rho-associated coiled-coil kinase）は，セリン・スレオニンリン酸化酵素で，アクチン細胞骨格再構成にかかわるRhoの下流シグナルを形成する分子量約160 kDaの小分子グアノシン3リン酸（GTP）結合蛋白質であり[1]，他臓器での報告であるがROCKシグナル経路の異常活性がある病態へのROCK阻害薬の投与で血管拡張効果が示され，臨床応用されている[2,3]．リパスジル塩酸塩（以下，リパスジル）点眼薬は，緑内障患者に対して2014年10月に承認されたRho kinase阻害薬（以下，ROCK阻害薬）である．原発開放隅角緑内障における房水流出抵抗の主座である線維柱帯流出路のSchlemm管からの房水流出を促進することにより眼圧

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Eur Radiol
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CONTRAST MEDIA

Protective effect against repeat adverse reactions to iodinated contrast medium: Premedication vs. changing the contrast medium

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Received: 24 March 2015 / Revised: 6 July 2015 / Accepted: 14 September 2015

Abstract

Objectives The purpose of this study was to assess the protective effect of premedication and changing contrast media (CM) against repeat adverse reactions (ARs) to iodinated CM.

Methods Between January 2006 and September 2014, 771 cases with previous ARs to CM were administered CM. The same CM that had caused ARs previously was administered to 491 cases (220 without premedication [defined as the control group], and 271 with premedication [the premedication alone group]). A different CM from the previous CM was given to 280 cases (58 without premedication [the changing CM alone group], and 222 with premedication [the premedication and changing CM group]).

Results The control group had 61 repeat ARs (27.7%). The premedication alone group had 47 ARs (17.3%, $p<0.01$). The changing CM alone group had 3 ARs (5.2%, $p<0.001$). Three ARs (7.9%) were observed in 38 cases changing from one to another low-osmolar nonionic CM. Twenty cases with previous ARs to the high-osmolar CM and to the low-osmolar ionic CM showed no ARs. The premedication and changing CM group had 6 ARs (2.7%, $p<0.001$).

Conclusion Premedication prior to contrast for patients with previous ARs may be protective, however, changing CM was more effective.

Key Points

- *In patients with previous adverse reactions, changing contrast media is recommended.*
- *Premedication is unnecessary against previous reactions to high-osmolar or ionic CM.*
- *Changing from one to another low-osmolar non-ionic CM may be effective.*

Keywords Repeat adverse reaction · Hypersensitivity · Iodinated contrast media · Premedication · Safety

Abbreviations

CM contrast medium
AR adverse reaction

Introduction

Patients with a history of adverse reactions to iodinated contrast media (CM) are at increased risk for repeat adverse reactions to iodinated CM [1]. Patients with a history of severe hypersensitivity sometimes avoid subsequent iodinated CM. However, a variety of iodinated CM have been treated together to evaluate the risk factor, nonspecifically as "iodinated CM" [1, 2]. It has been unclear whether a history of adverse reactions to one of the iodinated CMs is a risk for the different iodinated CMs. Even if it is a history of adverse reactions to high-osmolar CM or low-osmolar ionic CM, we cannot be sure that the low-osmolar non-ionic CM will be safe.

For patients with a history of hypersensitivity for CM, it is recommended that they be premedicated with corticosteroids and antihistamines before receiving CM [3, 4]. Many studies in the literature suggest premedication can decrease the frequency of adverse reactions [4, 5]. However, those patients are

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ORIGINAL ARTICLE

Spatial anatomy of the round ligament, gallbladder, and intrahepatic vessels in patients with right-sided round ligament of the liver

Kenji Ibukuro[1] · Takaya Takeguchi[2] · Hozumi Fukuda[1] · Shoko Abe[1] · Kimiko Tobe[1]

Received: 21 September 2015 / Accepted: 28 March 2016 / Published online: 11 April 2016

Abstract
Purpose To analyze the vascular structure of the liver in patients with a right-sided round ligament.
Methods We reviewed 16 patients with a right-sided round ligament and 3 polysplenia and situs inversus patients with a left-sided round ligament who underwent multidetector row CT with contrast media. The patient population consisted of 13 men and 6 women (mean 62 years). We analyzed the axial and volume-rendered images for the location of the round ligament, gallbladder, portal veins, hepatic veins, and hepatic artery. The following imaging findings for the patients with polysplenia and situs inversus were horizontally reversed.
Results The prevalence of a right-sided round ligament with and without polysplenia was 75 and 0.11 %, respectively. The gallbladder was located to the right, below, and left of the round ligament in 27.7, 38.8 and 33.3 %, respectively. Independent branching of the right posterior portal vein was noted in 57.8 %. PV4 was difficult to identify in 36.8 %. The middle hepatic vein was located to the left of the round ligament. Two branching patterns for the lateral and medial branches of the right anterior hepatic artery were noted: the common (44.4 %) and separated types (55.5 %). Both of the right anterior hepatic artery and portal vein ramified into two segments; the lateral segment with many branches and the medial segment with a few branches.
Conclusions The right-sided round ligament divided the right anterior section into the lateral and medial segments based on the portal vein and hepatic artery anatomy.

Keywords Right sided round ligament · Liver · Anomaly · Polysplenia · CT · Portal vein

Introduction

Hochstetter described a case with the round ligament (ligament teres) attached to the right portal vein in 1886 [7]. The gallbladder was located to the left of the round ligament in this particular case, so it had also been called the left-sided *gallbladder* [15]. However, the gallbladder is embryologically located at the midline [2]; thus, the right-sided *round ligament* is the appropriate term for this anomaly [13]. Recently developed imaging modalities such as multi-detector row CT and echography could detect a right-sided round ligament, and associated case reports have increased recently.

Polysplenia is a rare but well-known anomaly of the spleen and includes various anomalies of abdominal organs such as the short pancreas, preduodenal portal vein, and situs inversus [4]. However, there only one report has demonstrated a corrected right-sided round ligament associated with polysplenia [4].

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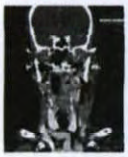
Table 1



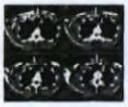


Table 2

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

Volume 28, Issue 4, July 2016, Pages 310–314

Case Report

Airway management in a patient with a deep neck abscess and tortuous brachiocephalic artery: Case report and review of the literature ☆

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Show more

http://dx.doi.org/10.1016/j.ajoms.2015.12.008

Abstract

Endotracheal intubation and tracheotomy under local anesthesia are available methods to maintain an adequate airway in patients with deep neck abscess; but neither of them is easy to perform. We report a case of deep neck abscess with a tortuous brachiocephalic artery in which massive hemorrhage from the pharynx occurred during endotracheal intubation. A 79-year-old man presented to our department with cervical swelling, hoarseness, and difficulty in swallowing. CT scans revealed abscesses associated with gas in the left submandibular space, left parapharyngeal space, and bilateral anterior cervical space. The brachiocephalic artery ran horizontally immediately beneath the thyroid gland on the anterior surface of the trachea. We decided to perform surgery under general anesthesia. Endotracheal intubation was selected to maintain an adequate airway, because tracheotomy was considered to be risky due to the high location of the brachiocephalic artery. Hemorrhage from the pharynx occurred immediately after insertion of a tracheal tube into the pharyngeal cavity. Bleeding was controlled by packing the pharyngeal cavity with gauze, after which the tube could be advanced into the trachea. Incisional drainage of the abscesses and debridement of necrotic tissue were performed. The patient was discharged from hospital 63 days postoperatively.

Keywords

Deep neck abscess; Tortuous brachiocephalic artery; Endotracheal intubation; Tracheotomy; Airway management

☆ Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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紹　介

“術後せん妄”に関するアンケート調査
—国立病院機構外科・麻酔ネットワークグループ—

七野　力[*1]　島川　宜子[*2]　渋谷　博美[*2]　鈴木　宏昌[*3]
小澤　章子[*4]　森脇　克行[*5]　平尾　素宏[*6]

キーワード：高齢者，術後せん妄，アンケート調査

要　旨

高齢者の術後せん妄について，多施設アンケートによる意識調査を行った。術後せん妄発症率は20-30%，発症時期は術後2日目，回復までに1カ月を要するという意見が多かった。発症のリスク因子としては，高齢，術後合併症，アルコール依存，精神障害，性別，麻酔深度などが，予防および治療としては，疼痛管理や生活リズムの改善，術後合併症の回避などが行われていた。術後せん妄のケアには多大な労力を必要とするという認識は共通していた。

急速に進む社会構造の高齢化とともに，外科学，麻酔科学の進歩に伴い，高齢者の手術件数は増加してきている。若年者に比べて高齢者は術後合併症の頻度が高く[1]，手術成績に大きな影響を及ぼす。なかでも術後せん妄は比較的高齢者に特有の合併症であり，手術成績のみならず医療資源や患者自身および医療従事者の安全上の観点からも大きな問題となる[2]。しかしながら，本邦においては術後せん妄に関する大規模な調査は現在まで行われておらず，その実態は明らかではない。実態調査の先駆けとして，国立病院機構外科・麻酔ネットワークグループでは40病院を対象に術後せん妄に関するアンケート調査を行ったので，その結果を報告する。

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麻酔 2016；65：756—762.

1. 方　法

2012年（平成24年）に国立病院機構外科・麻酔ネットワークグループに参加している40病院の代表者宛にアンケートを郵送した。締め切りまでの期間はおよそ1カ月とし，返送を依頼した。代表者は各施設で選出された外科系医師または麻酔科医であり，回答者は各施設代表者または代表者が指定した代理の外科系医師・麻酔科医とした。調査項目を表に示すが，主な内容は，回答者の術後せん妄に対する意識および各病院における実態ならびに対策に関するものとした。回答は選択形式で，リスクファクターや診断基準，対策，治療に関する選択肢は，成書および論文[3)~6)]を参考に決定した。なお本調査は外科医・麻酔科医の術後せん妄に対する意識調査であり，本質的に個人情報などは含まれないことから，厚生労働省“臨床研究に関する倫理指針”[7]に基づき，倫理審査委員会での審査は必要ないと判断した。

2. 結　果

26施設から回答を得，アンケート回収率は65%であった。代表回答者の診療科内訳は，一般外科17，麻酔科6，呼吸器外科2，心臓血管外科1であった。

高齢者の定義としては，75歳以上との回答が62%（16/26）と過半数を占めた（図1）。各施設が認識している高齢者の術後せん妄発症率は，中央値20-30%で10%未満から60-70%まで回答に大きな幅があった（図2）。術後せん妄の発症時期としては術後2日目，せん妄の回復までに要する期間は1カ月という回答が多かったが，術後せん

第4回 骨粗鬆症治療薬

患者に合った剤形を選択しアドヒアランス維持

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：ボナロン錠35mg/週を処方している患者が歯科を受診し，歯科医から休薬についての問い合わせがあったが，どうしたらいいのか？

：ボナロンのような窒素含有型ビスホスホネート（BP）製剤は，投与中に抜歯などの侵襲的歯科治療を受けた後に顎骨壊死の発生が報告されており，BP関連顎骨壊死（BRONJ）もしくは骨吸収抑制薬による顎骨壊死を総称してARONJと呼ばれています。侵襲的歯科治療前の休薬基準は投与期間およびリスクファクター（BP製剤の種類，治療内容，現病歴，薬歴など）の有無により異なります（表1）。
投与期間が3年未満でリスクファクターがなければ原則休薬は不要ですが，投与期間が3年以上もしくはリスクファクターがある場合，骨折リスクが高くなければ休薬が望ましいです。休薬が可能なら3カ月程度，治療後の投与再開は急ぐ場合には2週間後，余裕があれば2カ月前後で行います。

ポイント

わが国は超高齢社会を迎え，高齢者の骨粗鬆症に伴う骨折は医療においてのみならず社会的にも重要な課題となっている。骨粗鬆症の治療は薬物治療が主体であり，アドヒアランスを向上させ骨量増加ならびに骨折予防に寄与することは，われわれ薬剤師に課せられた責務である。

腎機能の確認とアドヒアランス維持へのサポートが大切

高齢者の特徴として，腎機能をはじめとした生理機能の低下ならびに認知機能の低下がある。現在上市されている骨粗鬆症治療薬にはBP製剤，副甲状腺ホルモン製剤，選択的エストロゲン受容体モジュレーター（SERM），活性型ビタミンD_3製剤などがあるが，その多くが腎機能障害時に慎重投与，一部は禁忌となるため，腎機能の確認が必須となる。

認知機能の低下は，アドヒアランスの低下につながる恐れがある。現在では経口剤だけでも毎日投与製剤，週1回投与製剤，月1回投与製剤があり，注射剤においても自己注製剤や静注製剤など治療薬は多様化している。そのため，患者の理解力や家族のサポート体制を確認し，ライフスタイルに合わせた製剤の提案が必要になる。また，円背の高齢者ではBP製剤服用後に喉のつかえ感や，胸やけなどの消化器症状を訴える例もあり，これらの副作用により，アドヒアランスの低下を招くこともある。剤形を含めた薬剤の特徴を知り，患者一人ひとりに対して適正な薬剤選択がされているかの確認も必要となる。

BP製剤服用患者では口腔内を清潔に保つ

BP製剤は骨粗鬆症治療の主要な薬剤で，強い骨吸収抑制作用と骨密度増加作用を有する。BP製剤で注意が必要な副作用に顎骨壊死がある。高齢者は虫歯治療や歯周病などで抜歯が必要な場合も少なくない。このためBP製剤服用時には口腔内の清潔に加え，歯科を受診する際にその旨を主治医に相談するよう説明する必要がある。特に口腔衛生状態の不良は局所リスクファクターとして挙げられるため（表1）口腔内の清潔の重要性を認識してもらうことが大切になる。

骨粗鬆症患者の多くが高齢者であることを踏まえ，われわれ薬剤師は腎機能とアドヒアランスについて，特に注意して確認する必要がある。

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Expanding distributions of red back spiders and bites in Japan from 2011 to 2013

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Abstract: In Japan, fourteen bites by the red back spider, *Latrodectus hasseltii*, were reported in four hospitals between 2011 and 2013 in a survey of sentinel hospitals. The distribution of the spider and the areas in which patients were bitten by the spider both expanded geographically each year. Although fatalities or severely ill patients are yet to be reported in Japan, stockpiles of the antivenom and communication with the public and medical professionals should be considered.

Key words: Red back spider, spider bite, Japan

The red back spider, *Latrodectus hasseltii*, is one of the medically significant widow spiders (Isbister and White, 2004) that is found in diverse habitats in many countries (Shahi et al., 2011). The localized symptoms of a red back spider bite are pain, itchiness, and diaphoresis, and systemic symptoms include nausea, vomiting, headache, and malaise. In Australia, red back spider bites are common, with an estimated number of at least 5,000 cases each year (Isbister and White, 2004), and a fatal case was reported (Braitberg and Segal, 2009). Although the antivenom is often used for pain relief (Isbister et al., 2014) in Australia, the antivenom is still unapproved drug in Japan. Those unapproved drugs are must be imported by each clinicians under the Pharmaceutical Affairs law. According to inquiry in 2012, only five hospitals in Mie, Osaka, Okinawa and Fukuoka were reserved antivenom for severe cases (Seiwa sangyo, 2013). In Japan, since the discovery of the spider in Osaka in 1995 (Nihei et al., 2004), red back spiders have been identified in 34 prefectures in Japan from northern Honshu to Okinawa Island by 2014 (IIRG, 2006; Ori et al., 1996). Currently, over 80 envenomation cases were report since its first identification, with the antivenom administered to six patients (IIRG, 2006). However, as these reports were from specific areas, it is not clear how much areas are affected by red back spider and its bites in Japan. Thus, we conducted a survey against 470 sentinel hospitals for other disease to determine how red back spider and the patients with its bite spread geographically, and how many antivenum are used in Japan.

The sentinel hospitals, as defined, were designated by local government, served a population of 75,000, and had 300 beds or more. The survey was conducted from January to March 2014, and collected information on the prefecture of the hospital, the number of beds, and the numbers of spider bites and red back spider bites, whether the patient was admitted, use of antivenom and fatality. We used reports from academic meetings, papers, and websites of local governments to identify prefectures in which the red back spider was found from 2011–2013. Approval for ethical protocols was not required

当院における急性心筋梗塞患者に対する外来心臓リハビリテーションの参加率と継続率

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池戸利行 1)，杉本圭子 3)，飯塚祐美子 4)，内田美子 5)，田邊潤 6)，梅本琢也 7)

要旨

【目的】当院における急性心筋梗塞(AMI)患者に対する外来心臓リハビリテーション(心リハ)の参加率及び継続率を調査し，今後の取り組みを考察すること．【対象】AMIにて入院し，入院期の心リハを実施した89例とした．【方法】外来心リハの参加の有無と4ヶ月間の継続の有無を調査し，それぞれの患者背景因子を比較検討した．また，外来心リハの不参加と非継続の理由も調査した．【結果】外来心リハ参加率は42.6%であり，外来心リハに参加した患者の4ヶ月間の継続率は78.5%であった．外来心リハ不参加例の年齢と脳血管疾患の既往を有する割合は，参加例と比較して有意に高値を示した(それぞれ$p<0.05$)．外来心リハ非継続例の脳血管疾患の既往を有する割合は，継続例と比較して有意に高値を示した($p<0.05$)．【結語】入院期の心リハを実施したAMI患者の約4割が外来心リハに参加し，4ヶ月間の外来心リハの継続率は約7割であった．高齢や脳血管疾患を合併している患者への対応が今後の課題であると考えられた．

キーワード：外来心臓リハビリテーション，参加率，継続率

1. はじめに

近年，急性心筋梗塞(acute myocardial infarction：AMI)患者に対する急性期治療は，緊急の経皮的冠動脈形成術(percutaneous coronary intervention：PCI)の実施が可能な施設が増加していることから，治療成績は飛躍的に向上している[1]．このことから，心機能障害は軽度で，早期退院が可能となるAMI患者が増加している．しかし，AMI患者の遠隔期にはPCI治療部位以外の新規病変に由来する再発が多いことが報告されており[2]，AMI患者の回復期は冠動脈を含む動脈硬化の進展を予防することが重要であるとされている[3]．その一方で，AMI後の救命率の向上に伴い，心機能障害が重度で心不全の合併を来す患者も存在し，このような患者に対しては退院後の心不全の管理も必要とされている[3]．

一方，心臓リハビリテーション(心リハ)はAMI患者の二次予防に効果的であることが知られており[4]，日本循環器学会のガイドラインにおいてもクラスⅠとして実施が推奨されている[3]．また，Hammillらの報告によると，外来心リハへの参加回数が多いほど予後が良好であることが示されており[5]，二次予防において，積極的な外来心リハの導入と長期間の継続が極めて重要となると考えられる．しかし，本邦における外来心リハの参加率は欧米諸国と比較して低いことが報告されている[6]．また，外来心リハの継続が困難となる患者も少なくない[7]．これまでに外来心リハの不参加例や非継続例の患者の特徴は先行研究で報告されているが[8,9,10]，地域や施設の特性によりその特徴は異なると思われる．そこで本研究は，当院におけるAMI患者の外来心リハの参加率と継続率を向上させることを目的に，外来心リハ不参加例と非継続例の患者の特徴を明らかにすることとした．

2. 対象および方法

a) 対象

2011年10月から2013年9月の間に，静岡医療センターにAMIの診断で入院しPCIを施行後，入院期

1）国立病院機構静岡医療センター ，2）常葉大学健康科学部理学療法学科，3）国立病院機構静岡医療センター看護師，4）同センター管理栄養士，5）同センター臨床心理士，6）同センター循環器内科医師，7）同センター心臓血管外科医師

原著

皮膚組織における終末糖化産物の蓄積と骨格筋量との関係

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加藤　倫卓[3)]　仁瓶　史美[2)]　竹田　義彦[4)]

抄　録

【目的】加齢とともに増加する終末糖化産物（AGEs）の蓄積が、骨格筋のタンパク質の機能を変化させることが報告されている。本研究の目的は、皮膚組織におけるAGEsの蓄積と骨格筋量との関係を調査することである。

【方法】対象は、健康診断を受診した中年および高齢の男女70名（58±10歳、男性55%）とした。対象の背景として年齢、性別、body mass index（BMI）、合併症および血液生化学検査の情報をカルテから調査した。皮膚組織におけるAGEsの蓄積の指標として、AGE Readerを用いてskin autofluorescence（SAF）を、骨格筋量の指標として、2重エネルギーX線吸収測定法を用いて骨格筋指数（SMI）を、筋力の指標として、握力を測定した。SMIと各調査項目との関係を、Pearsonの積率相関係数とSpearmanの順位相関係数を用いて解析した。また、SMIに独立して関係する因子を抽出するために、SMIを従属変数、年齢、性別、血清クレアチニン（Cr）、グリコヘモグロビンおよびSAF等を独立変数としてステップワイズ重回帰分析を行った。

【結果】SMIと有意な相関があった項目は年齢、性別、BMI、中性脂肪、Cr、握力およびSAFであった（それぞれ、r=0.312、P=0.011；r=-0.692、P<0.001；r=0.607、P<0.001；r=0.302、P=0.028；r=0.464、P<0.001；r=0.741、P<0.001；r=-0.413、P<0.001）。重回帰分析の結果、SAFと性別が独立してSMIと関係する因子として抽出された（それぞれ、P<0.001）。

【考察】中年および高齢の男女において、SAFは性別と共に独立してSMIに関係する因子であった。

（総合健診．2016；43：537-542.）

キーワード　骨格筋量、終末糖化産物、skin autofluorescence、サルコペニア

▶▶▶ 背　景

骨格筋量は、加齢とともに低下することが知られている。加齢に伴う骨格筋量の低下は、握力や歩行速度とともにサルコペニアを評価する際の指標のひとつとされている[1)]。先行研究によると、サルコペニアを有する高齢者は、日常生活活動（ADL）の低下や、転倒による骨折が多いことが報告されている[2)]。よって、加齢に伴う骨格筋量の低下に影響する要因を明らかにしサルコペニアに対する予防的戦略を立てることは、高齢者のADLを保つうえで極めて重要であると考えられる。

近年、加齢とともに増加する終末糖化産物（AGEs）の蓄積が、骨格筋のタンパク質の機能を変化させることが報告されている[3)]。AGEsはタンパク質、脂質および核酸が非酵素的に糖化されて形成される高分子であり、他のタンパク質に架橋を形成する特徴がある[4)]。骨格筋内に架橋が形成されると、骨格筋は硬化して筋力の低下を生じることが報告されている[3)]。さらに、AGEsは骨格筋量の減少を加速させることが、動物研究で明らかとされている[5)]。しかし、AGEsと骨格筋量の関係をヒトで検討した報告は少ない。

先行研究によると、何種類かのAGEsは特徴的な蛍光機能を有することが報告されており、ヒトの皮膚を蛍光測定することによって、上皮および真皮を含む皮膚組織に沈着したAGEs（skin autofluores-

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1）医療法人財団百葉の会銀座医院検査科
2）医療法人財団百葉の会銀座医院抗加齢センター
3）常葉大学健康科学部静岡理学療法学科
4）医療法人財団百葉の会銀座医院内科

Stretching Exercises Improve Vascular Endothelial Dysfunction Through Attenuation of Oxidative Stress in Chronic Heart Failure Patients With an Implantable Cardioverter Defibrillator

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■ **PURPOSE:** Endurance training improves oxidative stress and vascular endothelial dysfunction in patients with chronic heart failure (CHF). However, patients with CHF and an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D) often avoid endurance training for fear of ICD shock. Recent studies have reported that stretching exercises enhance antioxidant activity and improve vascular responses. Therefore, we aimed to assess the effects of 4 weeks of stretching exercises on oxidative stress and vascular endothelial function in patients with CHF with an ICD or CRT-D.

■ **METHODS:** Fifty sedentary patients with CHF (78% males; mean age = 70 ± 9 years; left ventricular ejection fraction = 26% ± 8%) with an ICD or CRT-D were randomly divided into a group that performed 4 weeks of stretching exercises (stretching group) and a group that continued a sedentary lifestyle (control group). We compared the reactive hyperemia peripheral arterial tonometry (RH-PAT) index and blood parameters, such as von Willebrand factor (vWF), malondialdehyde-modified low-density lipoprotein cholesterol (MDA-LDL), reactive oxygen species (ROS), high-sensitivity C-reactive protein, pentraxin 3, and fibrinogen between the 2 groups before and after the 4-week study period.

■ **RESULTS:** In the stretching group, a significant increase in the RH-PAT index and significant decreases in vWF, MDA-LDL, ROS, and fibrinogen concentrations were observed after the study compared with before (all $P < .05$). No significant changes were observed in the control group.

■ **CONCLUSION:** Four weeks of stretching exercises improved vascular endothelial dysfunction through attenuation of oxidative stress in sedentary patients with CHF with an ICD or CRT-D.

K E Y W O R D S

chronic heart failure

oxidative stress

stretching exercises

vascular endothelia function

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ベラパミル感受性心室頻拍

ベラパミル感受性心室頻拍の回路の特徴を理解してアブレーションしましょう。

Point

まずはこれだけ押さえよう

1 特徴的なP1電位とP2電位を理解しましょう。

2 アブレーションのターゲットはP1電位とP2電位の同時記録部位です。

3 マッピング，アブレーションの際の注意点を理解してからセッションに臨みましょう。

ベラパミル感受性心室頻拍の診断

●ベラパミル感受性心室頻拍は，明らかな心疾患の既往のない症例に発症します。発作時の体表面心電図記録では右脚ブロック＋上方軸偏位(左軸または北西軸)，まれに(10%程度)下方軸偏位のQRS波形を示します。上方軸偏位の場合は左脚後枝近傍，下方軸偏位の場合は左脚前枝近傍に起源があります。心室頻拍ではありますが，QRSの幅が130～160msecと比較的短いことが特徴です(**図1**)。

●"ベラパミル感受性"とは少量から中等量のベラパミル投与(経静脈投与)によって頻拍が徐拍化あるいは停止することを表していますが，ベラパミルのみに反応するわけではなく，Naチャネル遮断薬によっても同様に徐拍化・停止されます。本項では一般的な上方軸偏位のベラパミル感受性心室頻拍のアブレーション治療について述べます。

ベラパミル感受性心室頻拍の回路

●本頻拍の機序はリエントリーです。リエントリー回路はまだ完全に解明されていませんが，ベラパミルに反応する緩徐伝導特性のある構造物・Purkinje網が関与していることが想定されています(仮性腱索がその構造物であるとの報告があります)。

●この頻拍に関するマイルストーンとなった野上らの論文[1]では，マッピングカテーテルを左室中隔の心基部中部から心尖部下側部へ沿わせるように留置すると(**図2**)，頻拍中には緩徐伝導を有する組織を反映するP1電位(拡張期電位ともよばれます)と正常Purkinje電位を反映するP2電位(前収縮期電位ともよばれます)が記録され，P1は心基部から心尖部方向(近位から遠位へ)，P2は反対に心尖部から心基部へと伝導していることが示されています(**図3a**)。一方洞調律中には，左脚後枝領域のPurkinje線維の興奮がHis束よりも遅れて心基部から心尖部方向へ記録されています(**図3b**)。

Ⅲ 薬物治療の実践

6 致死的不整脈

POINT
1. アミオダロン静注薬はすべての機序の不整脈に抗不整脈効果を示す.
2. ニフェカラントはリエントリー性不整脈に抗不整脈効果を示す.
3. リドカインよりもⅢ群薬の使用が推奨される.

はじめに

心不全患者では心室頻拍 ventricular tachycardia・心室細動 ventricular fibrillation (VT/VF) の発症率が高いことが知られている. 実際, 心不全患者の多数を占める NYHA 分類 Class Ⅰ～Ⅲ患者の主要死因は VT/VF であり[1], 心不全治療を行ううえで心室性不整脈への対策は必須である.

本稿では実症例の提示から急性心不全に合併した VT/VF に対する急性期の薬物治療について解説する.

1 症例

a. 症例1(図1)

63歳男性. 急性心筋梗塞にて近医へ搬送後, 前壁部位の oozing rupture を合併していたため当院へ緊急手術目的に紹介となった. 心修復術後, 集中治療室で心不全の加療を施行していたが術7日後に VF が出現し, 心肺蘇生術を施行しながら電気的除細動 (DC ; direct current) を施行した. 心不全に対するカテコラミン投与および低カリウム血症が原因と考えられ, カテコラミンの減量とカリウムの補正を行った. しかし, 翌日には220 bpm の VT が出現した. 血圧は80台であり, DC の準備をしながらアミオダロンの静注 (150 mg の初回ボーラス投与と600 mg/日の持続静注) を施行した. アミオダロンの静注により VT は停止, 心室期外収縮との二段脈となり, その後心室期外収縮も消失した.

早期にアブレーション治療を行うほうが今後は望ましい.

VT/VF をいったん発症した患者の予後はきわめて悪く, 多くの臨床試験でも薬物治療による VT/VF 停止の有用性は示せても, 最終的な死亡率低下の有用性までは示されていない. このことは VT/VF を回避した後の全身管理の必要性を示唆しており, 集中治療における心不全管理のさらなる向上が必要とされている.

文献

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(小鹿野道雄)

Q33 高齢者の鎮静の注意点はなんですか？

Answer

鎮静でも注意すべきポイントは「**ABCDEが相互に肝腎**」である（表）．**高齢者ではすべての機能の低下と薬物代謝の遷延**により，容易に危機的状況に陥る可能性がある．

◆高齢者は増加している

WHO（世界保健機関：World Health Organization）は，65歳以上を高齢者と定義している．厚生労働省は65～74歳までを前期高齢者，75歳以上を後期高齢者とし，日本の高齢者の割合は20%で世界でも最も高い．高齢者の割合は今後も増加し，総務省統計局によると2015年には25%を超えると見込まれている[1]．

表 「ABCDEが相互に肝腎」

	鎮静前・中・後	高齢者での注意点	注意を要するその他の病態
A：Airway（気道）	常に観察と評価を怠らないこと	誤嚥のリスク	肥満，小児
B：Breathing（呼吸）		呼吸抑制時の代償能力低下	呼吸器疾患合併，肥満
C：Circulation（循環）		反応遅延，代償能力低下	循環器疾患合併
D：Dysfunction of central nervous system（中枢神経障害）		中枢神経抑制薬に対する感受性の上昇 譫妄，錯乱の頻度増加	
E：Environment（環境）	環境整備は必須 場所，モニタ，人的パワー	体温調節能低下	
相互に	鎮静薬and/or鎮痛薬	相互作用	特殊な薬物代謝，相互作用
肝		代謝低下，作用時間延長	肝硬変
腎		作用時間の延長	腎不全

● A：Assessment（評価）：施行後の評価，管理

①回復室での観察～移動中，病棟または帰宅後の患者の状態を予測する．高齢者は薬剤の効果が遷延する

②特殊事例はチームでデブリーフィング ⇒記録（記憶）に残すことは，管理の質の向上につながる

Point

- ☑ 鎮静でも「ABCDEが相互に肝腎」である．
- ☑ 高齢者ではすべての機能が低下しており容易に危機的状況に陥る．リスクを把握し状況を予測する．
- ☑ PDCAサイクルで「鎮静の計画―実行―確認―評価」を習慣づける．

〈小澤章子〉

編集後記

平成 28 年度の業績集が完成いたしました。日常診療が忙しいなか、臨床研究および治験に多大な努力をされている先生方に改めて敬意を表したいと思います。そして治験管理室看護師の井上満智代さん、勝又祐美子さん、薬剤師の伊東正樹先生、いつもありがとうございます。休日返上で研修や会議に出席し努力する姿に頭が下がります。また受託研究審査委員会のメンバーのみなさん、特に外部委員の先生方にはお忙しいところ貴重なお時間をいただき、誠にありがとうございます。最後に事務の渡邉光子さん。今回もまた締切間際まで仕事が終わらない私のためにご迷惑をおかけしました。渡邉さんの多大なる努力なしでこの業績集は完成できませんでした。ここに改めて心より感謝の意を表したいと思います。本当にありがとうございました。

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