静岡医療センター研究業績集（25）

（2017 年度）

静岡医療センター臨床研究部

発刊の辞

2017 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方々のご努力のたまものと考えます。

受託研究の多さと英文論文数の多さには驚くばかりで、静岡医療センターの実力を改めて実感しております。また、二つの国立病院機構共同臨床研究が開始となり、今後、NHO 内の共同研究が盛んにおこなわれていくこととなると思います。

静岡医療センターは平成２９年１０月に国立病院機構静岡富士病院の機能を統合して再出発しました。これまで急性期医療のみでしたが、重症心身障害と神経難病に対する医療も加わりました。今後は、神経難病部門などの臨床研究が増えてくることが期待されます。

今後もわが静岡医療センター臨床研究部の業績はうなぎのぼりに増加していくことが期待されます。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。

2018 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　中野　浩

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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29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 H29年4月～H29年9月
神経難病治療研究室長	本間　豊	併任	神経内科医長 H29年10月～H30年3月

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。
昨年10月に静岡富士病院と統合し、新たに重症心身障害･神経難病医療が加わることになりました。
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 29 年度活動の概要

本年度は昨年度と比べて学会発表、論文発表ともに減少しております。欧文での論文発表数が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29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
膵がん切除後の補助化学療法における S-1 単独療法と S-1 と メトホルミンの併用療法の非盲検ランダム化第Ⅱ相比較試験（ASMET）	中野　浩（外科）	9.9 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	澤味小百合（看護師）	3.2 万円

６．受託研究に関する実績

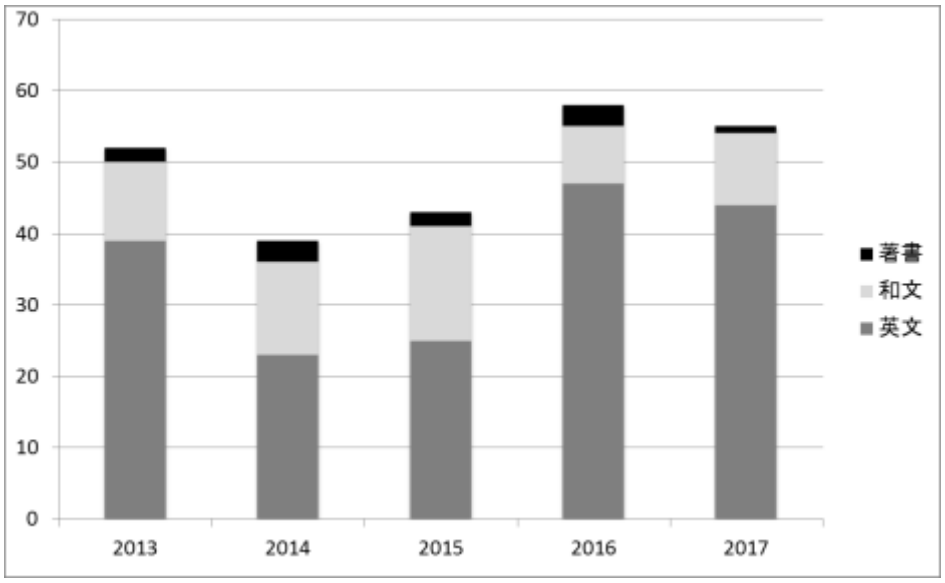
件　数	受託金額	実施率	治験審査委員会登録の有無
26件	22672 千円	42.8%	有

７．平成29年度の研究発表

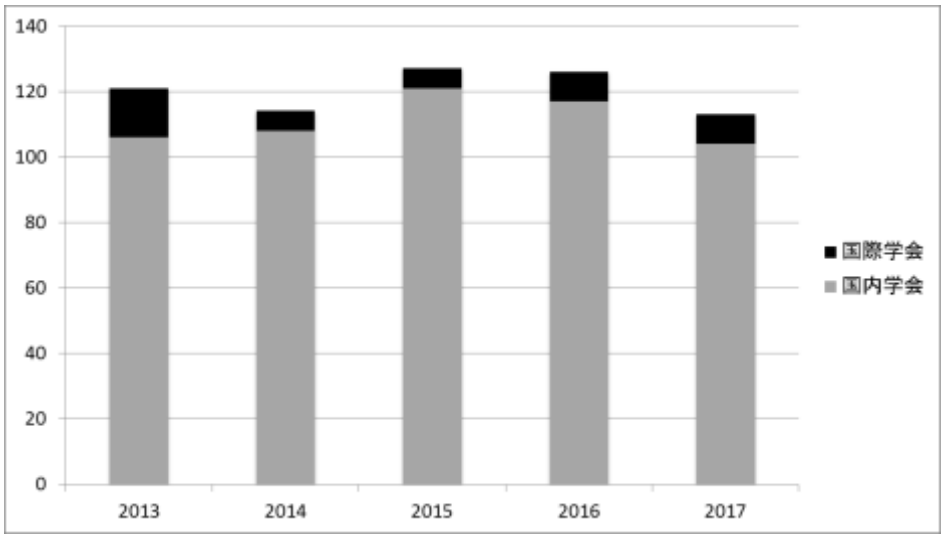
（１）学会発表：国内　104件、国際　9件、　　合計　113件
（２）論文発表：邦文　　10編、欧文 44編、　　合計　54編

※ 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	：	溝口　功一	（副院長）
委　　員	：	小澤　彰子	（統括診療部長）
委　　員	：	川中　秀和	（医局長）
委　　員	：	阿部　彰子	（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	：	成田　博	（企画課長）
委　　員	：	北山　淳一	（業務班長）

９．2017年度新規受託研究一覧

（１）治験

研究課題	依頼者	責任医師
M16-006 試験又は M15-991　試験の導入療法で改善したクローン病患者を対象として risankizumab の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照 52 週間維持療法試験及び非盲検継続投与試験	アッヴィ合同会社	消化器内科 部長 大西佳文
中等症からの重症の活動性クローン病患者を対象として risankizumab の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照導入療法試験	アッヴィ合同会社	消化器内科 部長 大西佳文
既存治療に対して効果不十分又は不耐容であるが生物学的製剤での治療失敗歴のない，中等症から重症の活動性クローン病患者を対象とした upadacitinib（ABT-494）の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照導入療法試験	アッヴィ合同会社	消化器内科 部長 大西佳文
生物学的製剤に対して効果不十分又は不耐容である中等症から重症の活動性クローン病患者を対象とした upadacitinib（ABT-494）の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照導入療法試験	アッヴィ合同会社	消化器内科 部長 大西佳文
M14-431 試験又は M14-433 試験を完了したクローン病患者を対象とした upadacitinib（ABT-494）の有効性及び安全性を評価する多施設共同無作為化二重盲検プラセボ対照維持療法及び長期継続投与試験	アッヴィ合同会社	消化器内科 部長 大西佳文

うっ血性心不全患者を対象としたトルバプタン錠経口投与 15mg に相当する OPC-61815 静脈内投与の用量を探索する多施設共同，無作為化，二重盲検，実薬対照，並行群間，臨床薬理試験	大塚製薬株式会社	循環器内科 臨床研究部長 田邊　潤
左室駆出率が低下した慢性心不全患者を対象に死亡及び罹病に対する omecamtiv mecarbil の有効性及び安全性を評価する二重盲検無作為化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
がん疼痛患者を対象とした HP-3150 の第Ⅲ相試験	久光製薬株式会社	外科 部長 角　泰廣
DU-176b 第 lll 相臨床試験（非弁膜症性心房細動）－既存の経口抗凝固薬の投与が困難な 80 歳以上の非弁膜症性心房細動患者を対象とした多施設共同無作為化プラセボ対照二重盲検比較試験―	第一三共株式会社	循環器内科 部長 小鹿野道雄
中等症から重症の活動性潰瘍性大腸炎患者を対象とした ABT-494 の導入療法及び維持療法における安全性及び有効性を評価する多施設共同無作為化二重盲検プラセボ対照試験	アッヴィ合同会社	消化器内科 部長 大西佳文
潰瘍性大腸炎患者を対象とした ABT-494 の長期安全性及び有効性を評価する第Ⅲ相多施設共同非盲検継続投与試験	アッヴィ合同会社	消化器内科 部長 大西佳文

（2）使用成績調査

研究課題	依頼者	責任医師
マヴィレット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
献血グロベニンーI 静注用水疱性類天疱病使用成績調査	日本製薬株式会社	皮膚科 部長 杉山由華
セララ錠使用成績調査 （慢性心不全を対象とした調査）	ファイザー株式会社	循環器内科 臨床研究部長 田邊　潤
シンポニー皮下注 50mg シリンジ シンポニーの潰瘍性大腸炎に対する特定使用成績調査	田辺三菱製薬株式会社	消化器内科 部長 大西佳文
プラリア特定使用成績調査関節リウマチ患者を対象とした長期使用に関する調査	第一三共株式会社	整形外科 部長 太田周介
レルベア 100 エリプタ特定用成績調査（COPD、長期）	グラクソ・スミスクライン株式会社	呼吸器外科 本橋典久
インフリキシマブ BS 点滴静注用 100mg「日医工」のクローン病及び潰瘍性大腸炎を対象とした長期の特定使用成績調査	日医工株式会社	消化器内科 部長 大西佳文

バリシチニブ（オルミエント R）特定使用成績調査既存治療で効果不十分な関節リウマチ患者を対象とした全例調査	日本イーライリリー株式会社	整形外科 部長 太田周介

（3）副作用詳細調査

研究課題	依頼者	責任医師
エリキュース副作用詳細報告	ファイザー株式会社	心臓血管外科 三ツ田翔平
「トリプレックス」の不具合等の調査	テルモ株式会社	心臓血管外科 院長 梅本琢也
グリセレブ配合点滴静注副作用詳細報告	テルモ株式会社	脳神経外科 部長 黒田勝宏
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

（4）医療機器

研究課題	依頼者	責任医師
XIENCE Alpine RX エベロリムス溶出型冠動脈ステントシステムに関する日本における市販後評価	アボットバスキュラージャパン株式会社	循環器内科 臨床研究部長 田邊　潤
ボストン・サイエンティフィックジャパン株式会社の販売する薬剤溶出型ステント『SYNERGY ステントシステム』及びガイドエクステンションカテーテル『GUIDEZILLA Ⅱ』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
ボストン・サイエンティフィックジャパン薬剤溶出型ステント／ガイドエクステンションカテーテル市場実態調査□	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

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）
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）
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委　　員：　成田　博　　（企画課長）
委　　員：　北山　淳一　（業務班長）

（１）当院にて実施研究

研究課題	研究責任者
TAZ/PIPC の長時間投与の有用性に関する検討	薬剤部 上田真也
ストレスのない経管栄養チューブの固定方法の検討	看護師 成川由衣
緩和病棟で働く看護師の困難度と今後の支援 ～困難度尺度を利用したアンケート調査より～	看護師 岩崎　舞
骨髄生検における CT での解剖学的評価	放射線科 五十嵐郁己
循環障害のある患者の創処置におけるテープ固定時の保湿剤使用の効果について	看護師 益子由美子
心臓デバイス装着患者における MR 検査の施行体制の検討	放射線科 診断部長 阿部彰子
本人または家族の行う嚥下スクリーニングと看護師の行う嚥下スクリーニングを比較し現在の課題について検討する	看護師 土原菜美
循環器病棟で勤務する看護師に対する意識調査	看護師 明智美苗

（２）多施設共同研究

研究課題	研究代表機関	研究責任者
病棟薬剤業務での疑義照会による有害事象回避事例件数の推移に関する多施設共同前向き観察研究（副題）有害事象回避事例率と病棟薬剤業務の成熟度の相関について	独立行政法人国立病院機構 熊本医療センター	薬剤部 薬務主任 内野達宏

放射線診療従事者の不均等被ばく、とくに水晶体の管理に関する実態調査	九州大学大学院医学研究院	中央放射線室 技師長 酒井一成
カテーテルアブレーションを施術した非弁膜症性心房細動症例の抗凝固療法の実態とその予後に関する観察研究	筑波大学循環器内科	循環器内科 部長 小鹿野道雄
2 型糖尿病合併急性心筋梗塞を有する患者の心突然死に対するエンパグリフロジンとプラセボのランダム化比較研究	日本医科大学付属病院	循環器内科 臨床研究部長 田邊　潤
深部静脈血栓症及び肺血栓塞栓症の治療及び再発抑制に対するリバーロキサバンの有効性及び安全性に関する登録観察研究	日本大学医学部 内科学系循環器内科学分野	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

2017 年度論文発表

【神経内科】

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A Japanese male with a novel ANO5 mutation with minimal muscle weakness and muscle pain till his late fifties.
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２）Hara D, Akiyama H, Nukui S, Shimizu T, Hoshikawa M, Hasegawa Y.
Utility of osteosclerotic lesion biopsy in diagnosis of POEMS syndrome.
A case report Medicine. 2017;Oct 96(41) 188

３）Sasaki R, Maki F, Hara D, Tanaka S, Hasegawa Y.
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【薬剤部】
１）稲葉真実、彦坂麻美、薄　雅人、滝　久司、小林智晴、大西佳文
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８）市川竜太郎
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２）高嶋志保、市川智子、三原奈未、杉本莉加、杉本圭子、森　雄司、内田美子、森下真理子、柴田晋弥、小鹿野道雄
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５）安田勢津子、岩崎　舞、鈴木里彩、高木幸子、飯田順子
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９）成川由衣、小嶋友理子、豊永なつみ、鈴木綾香、上坂洋子、野嶋弘美
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１５）岩崎　舞、安田勢津子、鈴木里彩、高木幸子、飯田順子
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- 自己調整学習の視点から -
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２）内田ゆかり、内田美和子、山口紀子
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- ペーパーペイシェントを活用して -
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【臨床工学技士室】
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１）森本大輔、加藤倫卓、光地海人、森　雄司、濵　貴之、千崎史顕、
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２）内藤裕治
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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。

Format: Abstract

Neuromuscul Disord. 2017 May;27(5):477-480. doi: 10.1016/j.nmd.2017.01.012. Epub 2017 Jan 18.

A Japanese male with a novel ANO5 mutation with minimal muscle weakness and muscle pain till his late fifties.

Kadoya M[1], Ogata K[2], Suzuki M[3], Honma Y[3], Momma K[3], Yatabe K[3], Tamura T[3], Kaida K[4], Miyata N[5], Nishino I[6], Nonaka I[7], Kawai M[3].

Author information

Abstract

Limb girdle muscular dystrophy type 2L (LGMD2L) is an adult-onset slowly progressive muscular dystrophy associated with anoctamin 5 (ANO5) gene mutation, mainly reported from Northern and Central Europe. We report the case of a Japanese male patient with a novel homozygous mutation of c.2394dup, p.Arg799Thrfs in ANO5 gene, the second patient in the Asian population. He had had marked elevation of creatine kinase (CK) level for more than 10 years with minimal muscular symptoms consisting of muscle stiffness and occasional cramps, preceding the onset of proximal limb weakness. Calf hypertrophy and selective fatty replacement of the adductor magnus and gastrocnemius muscles were prominent clinical and muscle imaging features. This case suggests that LGMD2L may affect a broader population than has been previously thought, physicians should consider the possibility of ANO5 mutation even in patients showing elevated CK level with no apparent muscle weakness but muscle stiffness or cramps.

KEYWORDS: Anoctamin 5; Calf hypertrophy; HyperCKemia; Limb girdle muscular dystrophy type 2L; Non-European population

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Utility of osteosclerotic lesion biopsy in diagnosis of POEMS syndrome

A case report

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Abstract

Rationale: We report a case of successful diagnosis of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome based on monoclonality that was confirmed by an osteosclerotic lesion biopsy in a patient without pathognomonic symptoms or monoclonal gammopathy, probably because of comorbidities, which included systemic lupus erythematosus, rheumatoid arthritis, and Sjögren syndrome.

Patient concerns: A 57-year-old woman presented with an approximately 2-year history of numbness in the toes that had gradually spread, along with muscle weakness in both arms and legs. She had been receiving immunosuppressant and corticosteroid therapy since being diagnosed with systemic lupus erythematosus and Sjögren syndrome at the age of 31 years and rheumatoid arthritis at the age of 44 years. Neurological examination revealed predominantly distal hypoesthesia and weakness in a typical stocking-and-glove pattern. Immunoelectrophoresis revealed elevated polyclonal immunoglobulin, which was attributed to her known underlying disease.

Diagnoses: Biopsy of an osteosclerotic lesion confirmed proliferation of monoclonal plasma cells, leading to a diagnosis of POEMS syndrome.

Interventions and outcomes: Lenalidomide therapy was started after the diagnosis and the patient had a favorable outcome.

Lessons: Osteosclerotic lesion biopsy can be useful for diagnosis of POEMS syndrome in difficult cases.

Abbreviations: CT = computed tomography, FLC = free light chain, MRI = magnetic resonance imaging, POEMS = polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SS = Sjögren syndrome, VEGF = vascular endothelial growth factor.

Keywords: osteosclerotic lesion, POEMS syndrome, rheumatoid arthritis, Sjögren syndrome, systemic lupus erythematosus

1. Introduction

POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome is a rare disorder with signs and symptoms that vary from one body site to another.[1] There are about 340 people with POEMS syndrome in Japan, indicating a prevalence of approximately 0.3 per hundred thousand population.[2] Furthermore, there is a few cases frequency of POEMS syndrome with collagen disease.[3–5] Proliferation of monoclonal plasma cells within an intramedullary plasmacytoma likely contributes to the pathology of POEMS syndrome. The condition is characterized by increased production of M-protein to a detectable level, an abnormal λ/κ free light chain (FLC) ratio, and obvious monoclonality (monoclonal gammopathy confirmed by immunoelectrophoresis).[1] Painless osteosclerotic lesions that are visible on plain skeletal radiography are also characteristic of POEMS syndrome. We report here a case of successful diagnosis of POEMS syndrome based on monoclonality (proliferation of monoclonal plasma cells) that was confirmed by an osteosclerotic lesion biopsy in a patient without pathognomonic symptoms or monoclonal gammopathy, probably because of comorbidities, which included systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and Sjögren syndrome (SS). Lenalidomide therapy was started after the diagnosis and the patient had a favorable outcome.

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Authorship: DH, HA, SN, and TS examined the patient, drafted the manuscript, and created the figures. MH performed the pathological examination. YH helped draft the manuscript. All authors read and approved the final manuscript.

The Human Research Ethics Committee of St. Marianna University Hospital provided a waiver considering that approval is not necessary for a single case report. Written informed consent was obtained from the patient.

The patient provided written informed consent for publication of clinical details and images. A copy of the consent form is available for review by the journal editor.

All relevant data are contained in the manuscript.

The authors declare that they have no competing interests.

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Cerebellum & Ataxias

Stratification of disease progression in a broad spectrum of degenerative cerebellar ataxias with a clustering method using MRI-based atrophy rates of brain structures

Rie Sasaki[†], Futaba Maki[*†], Daisuke Hara, Shigeaki Tanaka and Yasuhiro Hasegawa

Abstract

Background: The rate of disease progression differs among patients with degenerative cerebellar ataxia. The uncertain natural course in individual patients hinders clinical trials of promising treatments. In this study, we analyzed atrophy changes in brain structures with cluster analysis to find sub-groups of patients with homogenous symptom progression in a broad spectrum of degenerative cerebellar ataxias.

Methods: We examined 48 patients including 21 cases of spinocerebellar ataxia (SCA), 17 cases of the cerebellar type of multiple system atrophy (MSA-C), and 10 cases of cortical cerebellar ataxia (CCA). In all patients, at least two sets of evaluations including magnetic resonance imaging (MRI) and the International Cooperative Ataxia Rating Scale (ICARS) scoring were performed. The median number (min-max) of follow-up studies in each patient was three (2–6), and the mean follow-up period was 3.1 ± 1.6 years. The area of the corpus callosum on midsagittal images and the cerebellar volume were measured using MRI, and these values were divided by the cranial antero-posterior diameter of each patient to correct for individual head size differences as an area index (Adx) and a volume index (Vdx), respectively. The annual changes in Adx, Vdx, and ICARS score were calculated in each patient, and atrophy patterns in patients were categorized with cluster analysis.

Results: The annual atrophy rates for the corpus callosum (Adx) and cerebellum (Vdx) and symptom progression differed significantly by subtype of cerebellar ataxia (p = 0.026, 0.019, and 0.021, respectively). However, neither the annual atrophy rate of Adx nor Vdx was significantly correlated with the annual increase in the ICARS score. When the patients were categorized into three clusters based on the annual changes in Adx and Vdx, the annual increase in the ICARS score was significantly different among clusters (2.9 ± 1.7/year in Cluster 1, 4.8 ± 3.2/year in Cluster 2, and 8.7 ± 6.1/year in Cluster 3; p = 0.014).

Conclusions: The annual increase in the ICARS score can be stratified by cluster analysis based on the atrophy rates of the corpus callosum and cerebellum. Further studies are warranted to explore whether these simple MRI methods could be used for random allocation of a broad spectrum of patients with degenerative cerebellar ataxia in clinical trials.

Keywords: MRI, Cerebellar volume, Spinocerebellar degeneration, Multiple system atrophy, Corpus callosum, Spinocerebellar ataxia, Cluster analysis

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◆症例報告◆ 脳卒中 40: 24–28, 2018

前多血期に主幹動脈閉塞を伴う脳梗塞を発症し，数年後にcrescendo TIAを呈したJAK2V617F変異遺伝子陽性真性多血症の1例

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星野　俊[1)]　貫井　咲希[1)]　伊佐早健司[1)]　長谷川泰弘[1)]

要旨：症例は65歳女性．58歳時に頭蓋内主幹動脈狭窄を伴う脳梗塞を発症しシロスタゾールが開始された．62歳時に初回とは対側に脳梗塞が再発し，クロピドグレル，アスピリンへ変更となった．65歳1月時にJAK2V617F変異遺伝子が確認されたが，血球数増多が軽度のため真性多血症の診断には至らなかった．同年6月にクロピドグレル単剤へ減量，その約2カ月後に一過性喚語困難，呂律障害を繰り返し，crescendo TIAの診断で入院となった．入院後に真性多血症の診断となり，瀉血療法，シロスタゾール，ハイドロキシウレアの内服追加後に症状は消失した．真性多血症は脳梗塞のリスクとして知られているが，発症メカニズムは不明な点が多い．本症例は血球数増多を来す以前から頭蓋内主幹動脈狭窄を伴う脳梗塞を繰り返しており，JAK2V617F変異遺伝子の関与が推定され，文献的考察を含めて報告する．

Key words: JAK2 gene, polycythemia vera, cerebral infarction, crescendo TIA, antiplatelet agents

はじめに

真性多血症(polycythemia vera: PV)は骨髄増殖性疾患(myeloproliferative neoplasm: MPN)の一つであり，JAK2V617F変異遺伝子が95%以上の患者で検出されることから，同遺伝子変異が発症に関連していることが明らかとなっている[1)]．一方，PV患者の16～20%に脳梗塞，一過性脳虚血発作などの虚血性脳血管障害を来すとされ[2,3)]，その原因として血球数増多に伴う血液粘度の上昇，血球機能異常などが報告されてきたが，近年JAK2V617F変異遺伝子が血管内皮細胞障害を惹起して血栓症発症に至る新たな機序についても示唆されるようになった[1)]．今回，JAK2V617F変異遺伝子を背景に，血球増多が軽度であるPVの前多血期に，頭蓋内主幹動脈狭窄を伴う脳梗塞の再発，crescendo TIAが生じた1例を経験したので報告する．

症　例

患者：65歳，女性，右利き

主訴：言葉が出ない，呂律障害

既往歴：50歳時 高血圧，58歳時 脳梗塞(アテローム血栓性脳梗塞 右島皮質-前頭葉，右中大脳動脈M1起始部閉塞)，62歳時 脳梗塞，脂質異常症

嗜好歴：飲酒歴 機会飲酒，喫煙歴 なし

家族歴：特記事項なし

内服歴：クロピドグレル75 mg/日，アトルバスタチン10 mg/日，エナラプリルマレイン酸5 mg/日，アムロジピン10 mg/日

現病歴(Fig. 1)：62歳時に脳梗塞(左前頭葉-中心前回，左中大脳動脈M1狭窄)が再発し当院へ入院となった．経食道心臓超音波検査を含め塞栓源検索，全身性凝固疾患の精査を施行したが，明らかな異常は認めなかった．アスピリン100 mg/日，クロピドグレル75 mg/日へ抗血小板剤を変更し，ごく軽度の喚語困難が後遺症として残存したが自宅退院となった．頭部MRI上，頭蓋内主幹動脈狭窄が高度であることから，64歳時に抗血小板剤をシロスタゾール200 mg/日，クロピドグレル75 mg/日へ変更した．以前から軽度の血球数増多が継続するため，2015年1月に聖マリアンナ医科大学(以下，当院)血液内科を受診し，JAK2V617F変異遺伝子を有することが判明したが，血球数増多は軽度であり真性多血症の診断には至らなかった．同年6月にクロピトグレル

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原　著

肺炎球菌性髄膜炎に肺炎・感染性心内膜炎を合併したAustrian症候群の1例

原　大祐*　山徳　雅人*　佐々木　直*　篠原　健介*　長谷川泰弘*

〔要約〕症例は60歳男性．肺炎球菌性髄膜炎の診断で入院となった．髄膜炎は抗菌薬投与にて軽快するも，経胸壁，経食道心臓超音波検査で高度の大動脈弁逆流，逸脱を認めた．経過良好と考えられたが，第13病日より炎症所見の再燃，呼吸状態の悪化をきたし，急速に心不全症状が進行した．感染性心内膜炎による弁破壊，急性心不全と診断し，第22病日に大動脈弁置換術，大動脈基部形成術を施行した．術後経過は良好で，後遺症なく退院となった．肺炎球菌による肺炎，髄膜炎は適切な治療にもかかわらず時に致死的な感染性心内膜炎を合併することがあり，Austrian症候群として知られている．通常大酒家やcompromised hostなどに生じやすいとされるが，本症例ではこれらの危険因子はなかった．肺炎球菌感染では，危険因子の無い症例であっても本症を念頭において，心雑音の聴取などの注意深い身体所見の観察を行う必要がある．（神経治療 33：550-554，2016）

Key Words：Austrian syndrome, infectious endocarditis, bacterial meningitis, pneumonia, streptococcus pneumoniae

はじめに

肺炎球菌が起因菌となる髄膜炎は，成人例が大部分を占め，その約60%は何らかの基礎疾患を有している．近年，抗菌薬やステロイド療法の導入により救命率は向上しているが，その死亡率は17.7%と依然として高く，重篤な後遺症を残す例も23.8%に上る[1]．Austrian症候群とは肺炎球菌を起因菌とする肺炎，髄膜炎，感染性心内膜炎の3つを合併した症候群であり1957年に初めて報告された[2]．リスクとして中年男性，アルコール多飲，肝機能障害，薬物乱用，妊娠，分娩後女性やHIV患者，II型糖尿病，臓器移植後，脾摘後などが報告されている[3,4]．今回，我々は，特にリスクはなかったが，肺炎球菌性髄膜炎から肺炎を併発し，遅れて感染性心内膜炎を発症し救命し得たAustrian症候群の1例を経験したので，文献的考察を加えて報告する．

症　例

症　例：60歳，男性

主　訴：発熱，頭痛，意識障害

既往歴：気管支喘息（60歳時最終発作），好酸菌性中耳炎・副鼻腔炎，右耳感音性難聴あるが会話は可能．家族歴：特記事項なし

生活歴：飲酒 ビール350ml 2本/日×40年．喫煙歴なし．予防接種は肺炎球菌含め未施行．内服歴：theophylline 400mg/日，carbocysteine 1000mg/日，pranlukast hydrate 450mg/日，dexamethasone 0.1%5ml 1日2回両耳，budesonide/eformoterol fumarate dihydrate 60 dose 1回4吸入×2回/日［注］

現病歴：2014年8月中旬に滲出性中耳炎にて，当院耳鼻咽喉科で鼓膜切開術を施行した．耳漏培養で肺炎球菌陽性であり，抗菌薬加療後，prednisolone 30mg/日，20mg/日，10mg/日を各1日ずつ内服後に，点耳ステロイドを使用し問題なく経過していた．10月上旬に発熱，嘔吐を認め，4日後にトイレに起きた際に転倒した．妻の呼びかけに対して反応ないため救急搬送となり，同日精査加療目的で当科入院となった．

現　症：身長 167cm，体重 58kg，体温 40.0°C，血圧 184/106 mmHg，脈拍 108/分，SpO_2 97%（RA），呼吸数 16回/分．頭頸部では眼球結膜黄染なし，眼瞼結膜貧血なし，呼吸音は清，含気良好，雑音聴取せず．心音は整，第3肋間胸骨左縁で拡張期逆流性雑音（Levine II/VI）を聴取した．神経学的所見：意識障害（GCS E2V1M4 JCS III-100），項部硬直，Kernig徴候が陽性であった．脳神経系，運動系，感覚系，深部腱反射では明らかな異常は認められなかった．

入院時検査所見：血液学的検査では，WBC 10500/μl，T.Bil 1.0mg/dl，AST 110 IU/l，ALT 77 IU/l，LDH 286 IU/l，ALP 782 IU/l，γ-GTP 227 IU/l，Cre 1.06mg/dl，CRP 20.05mg/dl，プロカルシトニン 3.12ng/mlと炎症反応の上昇，肝機能障害，腎機能障害を認めた．脳脊髄液検査では，細胞数は81/μl（単核球 19/μl，多形核球 62/μl），蛋白濃度は163.6mg/dl，糖は1mg/dlであり，培養検査では，血液，髄液共に肺炎球菌が陽性であった．心電図，胸部X線，胸腹部CT，頭部CTでは異常所見はなかった．頭部MRIでは，拡散強調画像で側脳室下角周囲に炎症性細胞浸潤と考えられる高信号域を示し，FLAIR画像で両側側頭葉の脳溝の狭小化を認めた．

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Biallelic Mutations in *MYPN*, Encoding Myopalladin, Are Associated with Childhood-Onset, Slowly Progressive Nemaline Myopathy

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Nemaline myopathy (NM) is a common form of congenital nondystrophic skeletal muscle disease characterized by muscular weakness of proximal dominance, hypotonia, and respiratory insufficiency but typically not cardiac dysfunction. Wide variation in severity has been reported. Intranuclear rod myopathy is a subtype of NM in which rod-like bodies are seen in the nucleus, and it often manifests as a severe phenotype. Although ten mutant genes are currently known to be associated with NM, only *ACTA1* is associated with intranuclear rod myopathy. In addition, the genetic cause remains unclear in approximately 25%–30% of individuals with NM. We performed whole-exome sequencing on individuals with histologically confirmed but genetically unsolved NM. Our study included individuals with milder, later-onset NM and identified biallelic loss-of-function mutations in myopalladin (*MYPN*) in four families. Encoded MYPN is a sarcomeric protein exclusively localized in striated muscle in humans. Individuals with identified *MYPN* mutations in all four of these families have relatively mild, childhood- to adult-onset NM with slowly progressive muscle weakness. Walking difficulties were recognized around their forties. Decreased respiratory function, cardiac involvement, and intranuclear rods in biopsied muscle were observed in two individuals. MYPN was localized at the Z-line in control skeletal muscles but was absent from affected individuals. Homozygous knockin mice with a nonsense mutation in *Mypn* showed Z-streaming and nemaline-like bodies adjacent to a disorganized Z-line on electron microscopy, recapitulating the disease. Our results suggest that *MYPN* screening should be considered in individuals with mild NM, especially when cardiac problems or intranuclear rods are present.

Nemaline myopathy (NM) is a common form of congenital myopathy that is histologically defined by the presence of nemaline bodies within myofibers.[1] Typical clinical features include proximal-dominant muscle weakness, hypotonia, respiratory insufficiency, and bulbar weakness. It is not usually accompanied by ophthalmoplegia or cardiac dysfunction.[2] Mutations in genes encoding either a component of thin filament, such as *ACTA1* (MIM: 102610),[3] *NEB* (MIM: 161650),[4] *TPM3* (MIM: 191030),[5] *TPM2* (MIM: 190990),[6] *TNNT1* (MIM: 191041),[7] *CFL2* (MIM: 601443),[8] and *LMOD3* (MIM: 616112),[9] or proteins associated with thin filament stability or turnover, namely, *KBTBD13* (MIM: 613727),[10] *KLHL40* (MIM: 615340),[11] and *KLHL41* (MIM: 607701),[12] have been shown to cause NM, but the genetic cause remains unknown in 25%–30% of individuals with this disease.[12] The onset of the disease and its symptoms vary even among individuals with the same gene defect, but most affected individuals have delayed motor milestones and proximal-dominant muscle weakness involving facial muscle.[13] Intranuclear rod myopathy is a variant of NM in which rod-like inclusions are observed in myonuclei, often seen in the severe infantile form of NM with mutations in *ACTA1*.[14] Here, we present biallelic loss-of-function mutations in *MYPN* (MIM: 608517) in association with childhood-onset, slowly progressive NM with intranuclear rods.

Experimental protocols were approved by the local ethics committees (Yokohama City University School of Medicine for individual 1 and National Center of Neurology and Psychiatry for individuals 2–4). Written informed consent was obtained from all individuals or their parents. Clinical information was obtained from the medical records. The mouse study conformed to protocols approved by the Institutional Animal Care and Use

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名論

EUS

「静かな挿入」を心がけたEUS

Endoscopic ultrasonography (EUS) procedure with efforts at careful insertion

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key words：超音波内視鏡（EUS），超音波内視鏡挿入法

1 挿入前の心構え

超音波内視鏡（EUS）を成功させるためには，事前の心構えが大切である。

径の太いEUSスコープは直視下操作が不可能なため，より丁寧かつ慎重な操作が要求される。雑な挿入になった場合，消化管は激しく蠕動し，その結果，病変は不明瞭な画像となり正確な診断が得られない。EUSの特異性である高い空間分解能を発揮するためには，挿入前から静かな挿入と注意深い操作を念頭におくべきである。また精度の高い検査にするためには，描出すべき病変について，他の画像検査（CT，MRCPなど）との照らし合わせを事前に行っておくことも肝要である。病変の形態，特徴を検討しEUSに臨むことで，さらなる詳細な情報が得られ，高い診断能を享受できる。これらは，次の検査や治療へつながるものと考えられる。

2 挿入時に心がけていること

a. 口腔から食道まで

挿入はブラインドになるため，直視鏡挿入のイメージや感覚を思い描きながら挿入することが大切である[1]。被検者体位は左側臥位とし，鎮静後に左梨状窩を目標に挿入を始める。嘔吐反射を軽減するため，マウスピースの9時方向（左側臥位では天上側）に近づけながら，前方斜視型（コンベックス型）のプローブ面を被検者の足側に向くようにスコープをやや右捻り（時計回り）気味で挿入する。中咽頭から下咽頭後壁での通過はスコープを左捻り（反時計回り）に戻し，プローブ面と舌を全面に接触させながら進める。喉頭披裂に軽く触れるところでさらに左捻りし，ダウンアングルをかけながら進めると食道入口部を静かに通過することができる。挿入困難な場合は右梨状窩を目標にマウスピースの3時方向からの挿入を試みるが，これでも抵抗がある場合にはいったん直視鏡挿入に切り替え，挿入のイメージを再検討することも大切である。食道内では裂傷しないよう適度に送気し，ゆっくりと進める。

b. 胃から十二指腸まで

胃内では適度な送気と水洗により，粘膜の情報を見落とさないように心がける。EUSであっても内視鏡である以上，上部消化管病変を拾い上げることは内視鏡医の責務である。一方，幽門部ではできる限り脱気し静かに幽門輪を越えなければ，次の十二指腸球部での明瞭な画像は得られない。球部では脱気と送水の調和を配慮し，水平脚では左右上下アングルを軽く固定しながらストレッチする。左手はアップアングルを調節し，右手に全神経を集中させ，時計回転のトルクで微細かつ緻密な動きが可能となればEUSは成功する。

3 検査の引き際，止めどき

先端が硬いため粘膜損傷や穿孔の危険性に配慮して無理な挿入は控え，所用時間は20分前後を目安として被検者に負担の少ない検査[2]を心がける。

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特集 胆管内腔発育型腫瘍の概念と実態

胆管内，胆道内腫瘍（膵管内腫瘍との比較を含めて）

ICPN (Intracholecystic papillary-tubular neoplasms of the gallbladder)

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索引用語：胆嚢内乳頭状腫瘍，ICPN，前浸潤性病変，Rokitansky-Aschoff sinus（RAS）

1 はじめに

胆嚢における前癌病変（pre malignant lesions）が確立されつつある．前癌病変とは，正常組織よりも癌が発生しやすい状態へ形態学的に変化する病変のことであり，発癌母地とは異なる．胆管では，胆管内乳頭状腫瘍 intraductal papillary neoplasm of extrahepatic bile duct（IPNB）がすでに提唱されているが，WHO分類2010において，胆嚢の前癌病変，前浸潤性病変として胆嚢内乳頭状腫瘍 intracystic papillaryneoplasm of the gallbladder（ICPN）が位置づけられた[1]．しかしながら，画像診断，形態学的特徴，発育形式については熟知されておらず報告例も少ない．

ここでは，現在までの知見と自験例を含め，既報告例の文献的考察について述べることにする．

2 病名の概念と変遷

従来から頻度は少ないが，多数の呼称で知られている胆嚢前浸潤性乳頭状病変が，2010年WHO消化器腫瘍分類で，ICPNとadenomaに分類された．いずれもadenoma-carcinoma sequenceで進展していくという見解に基づいた分類である．膵IPMNの対比病変として胆管IPNBが提唱され，この概念を胆嚢にも応用したと考えられる（図1）．しかしながら，本文中[1]にもICPNとpapillary adenomaの鑑別は困難である，と不明確な表現で記載されている．そもそもこれは，胆嚢上皮が乳頭状構築を有しているため，平坦異型上皮であっても形態的には乳頭状腫瘍に視認しやすく，診断の再現性が低いためと考えられる．これらの混乱を解消すべく，2012年Adsayら[2]がICPNをintracholecystic papil-

Yoshifumi OHNISHI et al：Intracholecystic papillary-tubular neoplasms of the gallbladder
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特集 ER，ICUのための循環器疾患の見方，考え方
—エキスパートの診断テクニック—

Ⅰ．胸痛・背部痛

●各論 急性心膜炎

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Keywords: 急性心膜炎，心筋心膜炎

point

- 急性心膜炎の診断基準4項目の把握．
- 治療におけるコルヒチン併用の有用性．

急性心膜炎の鑑別/診断

急性心膜炎は心膜と心筋の外層である心外膜に急性炎症を起こす病態である．心電図変化を伴う胸痛で発症するため，急性心筋梗塞との鑑別を必要とする．急性心膜炎の診断はImazioらにより提案されており，4つの基準のうち，2つ以上を満たせば診断に至る[1]．その基準とは，①胸痛，②心膜摩擦音，③心電図における新規の広範な誘導でのST上昇もしくはPR低下，④心嚢液貯留である（表1）．また，白血球だけでなく，CRPや血沈などの炎症マーカーの上昇やCTおよび心臓MRIでの心膜の炎症所見も診断の一助となり，病勢の評価や治療の効果判定にも有用である[2]．胸部X線写真は正常であることが多く，その理由としては心嚢液が約300mL以上貯留しないと心胸郭比の増加を認めないからである[3]．以上のことから，急性心膜炎を疑う患者へは，心電図，心エコー，胸部X線写真，採血の検査が必須であり検査結果より鑑別と診断を行う．

表1 急性心膜炎の診断基準

以下の4項目のうち2つ以上を満たす

①胸痛

鋭い痛みで，前かがみで改善することが多い．85～90%で認められる．

②心膜摩擦音

胸骨左縁上で聴取しやすい，吸気呼気双方で認める．33%以下で認められる．

③心電図における新規の広範な誘導でのST上昇もしくはPR低下

ST上昇はaVR以外の全誘導で認め，凹型．鏡面像を認めないのが特徴．60%以上で認められる．

④心嚢液貯留

少量のことが多い．60%以上で認められる．

（文献1より引用）

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V．ショック・意識障害

●各論 心室頻拍・細動 (Brugada症候群等を含む)

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ventricular tachycardia/fibrillation (VT/VF)，鎮静，ニフェカラント，アミオダロン，硫酸マグネシウム，イソプロテレノール

point

- ショックや意識障害を伴うVT/VFはまず除細動を施行し，誘因の鑑別を早急に行い，治療を行う．
- 鎮静には抗不整脈効果がある．
- リドカインよりアミオダロン・ニフェカラントの使用が推奨される．
- 期外収縮後の長いポーズはVT/VFのリスクである．
- Brugada症候群に伴うVT/VFにはイソプロテレノールが有効である．

はじめに

救急・集中治療現場において心室頻拍・心室細動（ventricular tachycardia/fibrillation：VT/VF）が出現し，意識障害・ショック状態となればただちに救命処置として除細動治療を行うことが当然である．しかし，除細動治療はその場での対症療法にすぎず，VT/VFをその場で停止させても，その後のVT/VFの再発を予防する治療ではない．VT/VFの治療は除細動治療だけではなく，薬物加療・非薬物加療を含めた集学的加療を必要とする．

VT/VFをきたす主な要因として，心筋虚血，心不全，電解質異常（低K血症），感染・発熱，貧血，低酸素血症，QT延長などが挙げられる．これら要因に対する対処が結果的にVT/VFに対する治療となる．

急性冠症候群に合併するVT/VF

救急・集中治療の現場で急性冠症候群の患者が突然VT/VFを発症することがある．VT/VFの発症を予防するためには早急な冠動脈血行再建が優先されるが，状況がすぐに許容できない場面もある．VT/VF出現時で意識障害を伴う場合には，初期救急対応とし

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ORIGINAL ARTICLE

Suppression of aortic expansion and contractile recovery in a rat abdominal aortic aneurysm model by biodegradable gelatin hydrogel sheet incorporating basic fibroblast growth factor

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Abstract
Biodegradable gelatin hydrogel sheet (BGHS) incorporating basic fibroblast growth factor (bFGF) may inhibit the progression of abdominal aortic aneurysm (AAA). We investigated whether AAA in a rat model treated with BGHS soaked with bFGF can suppress aortic expansion and recover the contractile response of aneurysmal aortic wall. Experimental AAA was induced in 10-week-old male Sprague–Dawley rats with intra-aortic elastase infusion. Aortas of these rats were assigned to 4 groups ($n = 6$ each) as follows: Control group, aortas infused with saline; Elastase only group, aortas infused with elastase; Hydrogel group, aortas wrapped with saline-soaked BGHS after elastase infusion; and bFGF group, aortas wrapped with bFGF (100 μg)-soaked BGHS after elastase infusion. Preoperatively and on postoperative day (POD)7 and POD14, mean aortic maximal diameter was measured ultrasonographically. Aortic expansion ratio was calculated as: (post-infusion aortic diameter on POD14/pre-infusion aortic diameter × 100). Aortas were stained with Elastica van Gieson and α-smooth muscle actin to measure the ratio of elastic fibers and α-smooth muscle actin-positive cells area to the media area. Aortas on POD14 were cut into 2-mm rings and treated with contractile agent, then tension was recorded using myography. Maximum aorta diameters were significantly greater in Elastase only group, Hydrogel group, and bFGF group than in Control group (on POD14). Maximum diameter was significantly lower in bFGF group (3.52 ± 0.4 mm) than in Elastase only group (6.21 ± 1.4 mm on POD14, $P < .05$). On histological analysis, ratio of the area staining positively for elastic fibers was significantly greater in bFGF group (7.43 ± 1.8%) than in Elastase only group (3.76 ± 2.9%, $P < .05$). The ratio for α-smooth muscle actin-positive cells was significantly lower in Elastase only group (38.3 ± 5.1%) than in Control group (49.8 ± 6.7%, $P < .05$). No significant differences were seen between Elastase only group and bFGF group, but ratios tended to be increased in bFGF group. Consecutive mean contractile tensions were significantly higher in bFGF group than in Elastase only group. Maximum contractile tension was significantly higher in bFGF group (1.3 ± 0.4 mN) than in Elastase only group (0.4 ± 0.2 mN, $P < .05$). Aortic expansion can be suppressed and contractile responses of aneurysmal aortic wall recovered using BGHS incorporating bFGF.

Keywords Abdominal aortic aneurysm · Basic fibroblast growth factor · Angiogenesis · Vascular function

Introduction

Abdominal aortic aneurysm (AAA) is a potentially deadly disorder that has traditionally been treated primarily by surgical aortic replacement (SAR). In recent years, endovascular aortic repair (EVAR) has become more commonly utilized [1]. Unlike SAR that require laparotomy under general anesthesia, EVAR can be performed with an incision to the groin area to expose the artery (or insertion of a catheter) alone under local anesthesia. However, while the lesion site is resected in SAR, aneurysmal aortic wall is conserved

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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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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 disease (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

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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

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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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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 we 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 (ORs) 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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Key words: Cardiac surgical procedures - Meta-analysis - Seizures - Tranexamic acid.

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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A meta-analysis of effects of transcatheter versus surgical aortic valve replacement on left ventricular ejection fraction and mass

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ABSTRACT

Objectives: To determine which procedure, transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR), for severe aortic stenosis (AS) improves follow-up left ventricular (LV) function or hypertrophy more effectively, we performed the first meta-analysis of comparative studies reporting LV ejection fraction (LVEF) or mass (LVM) after TAVI versus SAVR.

Methods: Studies considered for inclusion met the following criteria: the article was written in English; the design was a comparative study; the study population was patients with severe AS; patients were assigned to TAVI versus SAVR; and outcomes included follow-up (6–12-month) LVEF or LVM. For each study, data regarding fractional changes in LVEF or LVM in both the TAVI and SAVR groups were used to generate mean differences (MDs) and 95% confidence intervals (CIs).

Results: Our search identified 8 eligible studies. Two studies with baseline LVEF < 40% demonstrated significantly greater fractional changes in LVEF after TAVI than after SAVR. A pooled analysis of 6 studies demonstrated no statistically significant difference in fractional changes in LVEF between TAVI and SAVR (MD, 3.25%; 95% CI, −1.30% to 7.80%; $p = 0.16$). Another pooled analysis of 5 studies demonstrated significantly greater fractional changes (i.e. less fractional "reductions") in LVM after TAVI than after SAVR (MD, 4.75%; 95% CI, 2.18% to 7.32%; $p = 0.0003$).

Conclusions: For patients with severe AS, SAVR may be associated with greater improvement in LVM, probably not in LVEF, at 6–12 months. For limited patients with reduced LVEF, TAVI might be associated with greater improvement in LVEF.

1. Introduction

Aortic stenosis (AS) is frequently accompanied by left ventricular (LV) hypertrophy (LVH) and remodeling [1]. Lower LV mass (LVM) is associated with lower rates of clinical end points such as cardiovascular death, fatal or nonfatal myocardial infarction, and fatal or nonfatal stroke [2]. A significant reduction in LVH occurs during the first 18 months after surgical aortic valve replacement (SAVR) for severe AS [3]. Insufficient regression of LVH is related to indices of irreversible myocardial disease, which also prevents functional LV improvement despite successful SAVR and a hemodynamically well-functioning valve [3]. It is still controversial whether incomplete regression of LVH is associated with poorer long-term survival [1]. Gaudino et al. [4] demonstrated that the extent of LVM regression after SAVR did not correlate with 28 ± 9-month survival. Whereas, Zybach-Benz et al. [5] indicated that LVH at 5.8 ± 5.4 years after SAVR was an independent predictor of cardiac-related morbidity. The introduction of transcatheter aortic valve implantation (TAVI) in clinical practice has widened options for symptomatic patients at high surgical risk [1]. However, it is not known whether TAVI has equivalent or prolonged benefits in terms of LV functional improvement and reverse remodeling [1]. No quantitative meta-analysis regarding this topic has been conducted to date. To determine which procedure, TAVI or SAVR for severe AS, improves follow-up LV function or LVH more effectively, we performed the first meta-analysis of studies comparing LV ejection fraction (LVEF) or LVM after TAVI with that after SAVR.

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; CABG, coronary artery bypass grafting; CI, confidence interval; CHOICE, Randomized Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT; EF, ejection fraction; LV, left ventricle; LVH, LV hypertrophy; LVM, LV mass; LVMI, LVM index; MD, mean difference; PARTNER, Placement of AoRTic TraNscathetER Valves; PPM, prosthesis-patient mismatch; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

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Meta-Analysis of Seasonal Incidence of Aortic Dissection

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We performed the first meta-analysis to identify in which season incidence of aortic dissection is the most and least frequent. MEDLINE and EMBASE were searched through February 2017. Eligible studies were observational studies enrolling patients with aortic dissection and reporting seasonal or monthly incidence of aortic dissection. Study-specific estimates, incidence of aortic dissection in each season (number of aortic dissection in a season divided by that in a year) and risk ratios (RRs) for incidence of aortic dissection in a season versus another season, were combined using the random-effects model. We identified 18 eligible studies enrolling a total of 101,264 patients with aortic dissection. Pooled incidence was 20.6% in summer, 24.8% in autumn, 28.2% in winter, and 25.5% in spring. Pooled analysis demonstrated a statistically significant increase in incidence of aortic dissection in autumn than in summer (RR 1.18; p <0.0001), in winter than in summer (RR 1.37; p <0.0001), in spring than in summer (RR 1.24; p <0.0001), in winter than in spring (RR 1.11; p = 0.006), and in winter than in autumn (RR 1.17; p <0.001); and no statistically significant difference between spring and autumn (RR 1.04; p = 1.00). In conclusion, the incidence in winter (28.2%) was significantly more frequent than that in other seasons and that in summer (20.6%) was significantly less frequent than that in other seasons (winter > spring ≈ autumn > summer). (Am J Cardiol 2017;120:700–707)

There is considerable evidence that several cardiovascular diseases, such as acute myocardial infarction, sudden death, supraventricular tachycardia, silent ischemia, pulmonary embolism, and stroke, are not randomly distributed but occur with chronobiologic periodicity.[1] Seasonal variation in morbidity and mortality due to cardiovascular diseases has been noted in both the northern and southern hemispheres, with higher incidence rates in winter than in summer.[2] Presence of rhythmic patterns in the incidence of acute aortic rupture or dissection (including not only acute aortic dissection [AAD] but also aortic aneurysm rupture), characterized by significantly higher risk in winter, is suggested.[3] In the present article, we performed the first meta-analysis to identify in which season incidence of aortic dissection is the most and least frequent.

Methods

All studies investigating seasonal incidence of aortic dissection were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through February 2017 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 *aortic dissection*; and *season(s)*, *seasonal*, *seasonality*, *monthly*, *chronology*, *chronologic*, *chronological*, *chronobiology*, *chronobiologic*, or *chronobiological*.

Studies considered for inclusion met the following criteria: the design was an observational study; the study population was patients with aortic dissection, and main outcomes included seasonal or monthly incidence of aortic dissection. Data were extracted in duplicate by 2 investigators (HT and TA) and independently verified by a third investigator (TU). Disagreements were resolved by consensus.

For each study, we generated risk ratios (RRs) and 95% confidence intervals for incidence of aortic dissection (1) in autumn versus in summer, (2) in winter versus in summer, (3) in spring versus in summer, (4) in winter versus in autumn, (5) in spring versus in autumn, and (6) in winter versus in spring using data regarding incidence of aortic dissection in each season. When only monthly incidence of aortic dissection was available, we defined summer, autumn, winter, and spring as June to August, September to November, December to February, and March to May, respectively. Study-specific estimates, incidence of aortic dissection in each season (number of aortic dissection in a season divided by that in a year), and the aforementioned RRs, were combined using the random-effects model. To counteract the problem of multiple comparisons, p values were adjusted by the Bonferroni correction.

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ORIGINAL ARTICLE

Perioperative depression or anxiety and postoperative mortality in cardiac surgery: a systematic review and meta-analysis

Hisato Takagi[1] · Tomo Ando[2] · Takuya Umemoto[1] · ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

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Abstract We performed a systematic review and meta-analysis to determine whether perioperative depression and anxiety are associated with increased postoperative mortality in patients undergoing cardiac surgery. MEDLINE and EMBASE were searched through January 2017 using PubMed and OVID, to identify observational studies enrolling patients undergoing cardiac surgery and reporting relative risk estimates (RREs) (including odds, hazard, or mortality ratios) of short term (30 days or in-hospital) and/or late all-cause mortality for patients with versus without perioperative depression or anxiety. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic RREs in the random-effects models. Our search identified 16 eligible studies. In total, the present meta-analysis included data on 236,595 patients undergoing cardiac surgery. Pooled analysis demonstrated that perioperative depression was significantly associated with increased both postoperative early (RRE, 1.44; 95% confidence interval [CI] 1.01–2.05; $p = 0.05$) and late mortality (RRE, 1.44; 95% CI 1.24–1.67; $p < 0.0001$), and that perioperative anxiety significantly correlated with increased postoperative late mortality (RRE, 1.81; 95% CI 1.20–2.72; $p = 0.004$). The relation between anxiety and early mortality was reported in only one study and not statistically significant. In the association of depression with late mortality, there was no evidence of significant publication bias and meta-regression indicated that the effects of depression are not modulated by the duration of follow-up. In conclusion, perioperative depression and anxiety may be associated with increased postoperative mortality in patients undergoing cardiac surgery.

Keywords Anxiety · Cardiac surgery · Depression · Meta-analysis · Mortality

Introduction

The number of patients undergoing coronary artery bypass grafting (CABG) affects by any depression (i.e., major, minor, or dysthymia) is approximately 30–40% of all cases, and an association with increased risk of morbidity in the short and longer terms is highlighted by a longstanding empirical interest on psychosocial factors in CABG patients [1]. In surgery patients suffering from a wide range of conditions, depression may be a frequent cause of morbidity [2]. Preoperative anxiety also may increase the risk of poor postoperative outcomes including atrial fibrillation, acute myocardial infarction, increased risk of readmission, increased morbidity and mortality, increased health care utilization, and increased anxiety in caregivers resulting in role strain and frustration [3]. Although the behavioral and biological mechanisms are poorly understood, both depression and anxiety are suggested to increase the risk for mortality and morbidity after CABG independent of medical factors [1]. In the present article, we performed a

The first and second authors (Hisato Takagi and Tomo Ando) contributed equally to this study and share the first authorship.

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Original Article

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A meta-analysis of weekend admission and surgery for aortic rupture and dissection

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Abstract

We performed a meta-analysis to determine whether weekend admission and surgery for ruptured abdominal/thoracic aortic aneurysm (RAAA/RTAA) and acute aortic dissection (AAD) is associated with increased mortality. MEDLINE and EMBASE were searched from January 1946 to December 2016 using PubMed and OVID. Eligible studies were prospective or retrospective, comparative or cohort studies enrolling patients admitting or undergoing surgery for RAAA/RTAA/AAD and reporting mortality after weekend (including holiday) versus weekday admission/surgery. Our search identified 11 studies including a total of 166,195 patients. A pooled analysis of 13 adjusted odds ratios (ORs), one adjusted hazard ratio, and one unadjusted OR from all 11 studies demonstrated a statistically significant 32% increase in mortality with weekend admission/surgery (OR, 1.32; 95% confidence interval (CI), 1.20 to 1.45; $p < 0.00001$). Despite possible publication bias disadvantageous to weekend admission/surgery based on funnel plot asymmetry, adjustment for the asymmetry using the trim-and-fill method did not alter the significant association of weekend admission/surgery with increased mortality (OR, 1.21; 95% CI, 1.09 to 1.34; $p = 0.0006$). In conclusion, weekend admission/surgery for ruptured abdominal/thoracic aortic aneurysm and acute aortic dissection (AAD) may be associated with increased mortality.

Keywords

abdominal aortic aneurysm (AAA), thoracic aortic aneurysm (TAA), acute aortic dissection, meta-analysis, mortality, weekend

Introduction

Patients with ruptured abdominal/thoracic aortic aneurysm (ruptured AAA/TAA (RAAA/RTAA)) and acute aortic dissection (AAD) may be admitted to the hospital and then undergo emergency or urgent surgery on off-hours including weekends, holidays, and nights due to the sudden onset of diseases. Because of a shortage of staff[1–3] and lack of experienced clinician expertise,[4] as well as inadequate subspecialty care[5] and therapeutic[6] or diagnostic procedures,[4] off-hour admission may be associated with increased mortality and other adverse outcomes,[7] which has been called the 'off-hour effect'.[8] A previous meta-analysis[7] of 251 cohorts from 140 articles (including six data sets from five studies[4,9–12] enrolling a total of 36,214 patients with aortic aneurysm) suggests that off-hour admission is associated with an increased mortality risk. Recent published studies, however, demonstrated no significant increase in mortality with weekend emergency/urgent open surgical repair (OSR) for AAA[13] and weekend admission for RAAA.[14] In the present article, we performed a meta-analysis to determine whether weekend admission and surgery for RAAA/RTAA/AAD is associated with increased mortality.

Materials and methods

Search strategy

All studies investigating associations of weekend admission/surgery for RAAA/RTAA/AAD with mortality were identified using a two-level search strategy. First, MEDLINE and EMBASE were searched from January 1946 to December 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 'weekend', 'aortic', and 'aneurysm', 'rupture', or 'dissection'.

Study selection and data extraction

Studies considered for inclusion met the following criteria: the design was a prospective or retrospective, comparative or cohort study; the study population was patients admitting or undergoing surgery for RAAA/RTAA/AAD; and outcomes

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Original communication

A meta-analysis of monthly variation in occurrence of abdominal aortic aneurysm rupture

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[a] These authors contributed equally to this paper

Summary: *Background:* We performed a meta-analysis to assess the presence of an annual rhythmic variability of ruptured abdominal aortic aneurysm (RAAA) onset. *Patients and methods:* Eligible studies were observational studies enrolling patients with RAAA and reporting monthly incidence of RAAA. Study-specific estimates, i.e. monthly incidence of RAAA, were combined using the random-effects model. Chronobiological analysis was performed by applying a partial Fourier series to pooled monthly incidence by using the weighted least-squares method. *Results:* We identified 14 eligible studies enrolling a total of 3,798 patients with RAAA. Pooled monthly incidence of RAAA was 8.7 % in January, 7.7 % in February, 8.7 % in March, 7.3 % in April, 7.8 % in May, 7.2 % in June, 7.0 % in July, 7.0 % in August, 8.1 % in September, 8.8 % in October, 8.4 % in November, and 8.3 % in December. Chronobiological analysis identified a significant ($p = 0.0020$) annual pattern in the occurrence of RAAA with a peak in December to January and a nadir in June to July. Pooled analysis demonstrated significantly more incidence in December than in June ($p = 0.03$) as well as in January than in July ($p = 0.05$). *Conclusions:* A significant annual pattern in the occurrence of RAAA with a peak in December to January and a nadir in June to July was identified with significantly more incidence in December than in June and in January than in July.

Keywords: Abdominal aortic aneurysm, meta-analysis, monthly variation, rupture

Introduction

The cardiovascular event occurrence is suggested not to be evenly distributed over time, but to show peculiar temporal patterns varying with time of day, day of week, and month (season) of year [1]. A clear seasonal trend in cardiovascular diseases (such as deep venous thrombosis, pulmonary embolism, aortic dissection, stroke, intracerebral haemorrhage, hypertension, heart failure, angina pectoris, myocardial infarction, sudden cardiac death, ventricular arrhythmia, and atrial fibrillation) exists with the highest incidence occurring during the colder winter months [2]. There are temporal patterns, characterized by circadian, weekly, monthly, and seasonal variations, in onset for aortic aneurysms similar to other acute cardiovascular events [3]. A recent meta-analysis [4] strongly supports the presence of evident rhythmic patterns, characterized by significantly higher risk in winter, in December, on Monday, and between 6 am and 12 pm, in the incidence of acute aortic rupture or dissection, including not only ruptured abdominal aortic aneurysm (ruptured AAA, RAAA) but also acute aortic dissection (AAD). Aetiology of AAA, however, is suggested to be distinct from that of aortic dissection. Synchronous existence of AAA and AAD is believed to be rare [5], and AAD develops in the absence of a preexisting aortic aneurysm in most (>80 %) cases [6]. Mechanisms for the rupture of AAAs and those for onset of aortic dissection may be not the same. In this article, we performed a meta-analysis to assess the presence of an annual rhythmic variability of exclusive RAAA onset.

Materials and methods

All studies investigating monthly incidence of RAAA were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through March 2017 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,

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ORIGINAL STUDIES

WILEY

Drug-eluting stents versus coronary artery bypass grafting for left-main coronary artery disease

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Abstract

Objectives: To compare follow-up outcomes after percutaneous coronary intervention with drug-eluting stents (DES-PCI) versus coronary artery bypass grafting (CABG) for left-main coronary artery disease (LMCAD), we performed a meta-analysis of randomized controlled trials (RCTs) and observational studies with propensity-score analysis.

Methods: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through November 2016. Eligible studies were RCTs or observational studies with propensity-score analysis of DES-PCI versus CABG enrolling patients with LMCAD and reporting ≥ 6-month mortality, myocardial infarction (MI), stroke, or repeat revascularization (RRV). Study-specific estimates were combined using inverse variance-weighted averages of logarithmic hazard ratios (HRs) in the random-effects model.

Results: We identified 5 RCTs and 17 observational studies with propensity-score analysis enrolling a total of 12,387 patients. Pooled analysis demonstrated a significant increase in a composite of death, MI, and RRV (with/without stroke) after DES-PCI (HR, 1.42; $P < 0.00001$); no significant difference in a composite of death and MI (with/without stroke); no significant differences in mortality and stroke; a strong trend toward an increase in MI after DES-PCI (HR, 1.44; $P = 0.05$); and significant increases in any (HR, 1.86; $P < 0.00001$), target-vessel (HR, 3.28; $P < 0.00001$), and target-lesion RRV (HR, 2.26; $P = 0.003$) after DES-PCI.

Conclusions: When compared with CABG, DES-PCI for LMCAD was associated with increases in RRV and the composite of death, MI, and RRV (with/without stroke), despite no differences in mortality, MI, stroke, and the composite of death and MI (with/without stroke).

KEYWORDS
drug-eluting stents, coronary artery bypass grafting, left-main coronary artery disease, meta-analysis

1 | INTRODUCTION

For several decades, coronary artery bypass grafting (CABG) has been considered the "gold standard" for left-main (LM) coronary artery disease (CAD) (LMCAD) revascularization in patients eligible for surgery [1,2]. More recently, however, percutaneous coronary intervention (PCI) has emerged as a possible alternative mode of revascularization [1]. Drug-eluting stents (DES) are suggested to be associated with favorable outcomes for mortality, myocardial infarction (MI), target-vessel/lesion (TV/TL) repeat revascularization (RRV) (TV-/TL-RRV), and major adverse cardiac events as compared with bare-metal stents (BMS) in PCI for LMCAD [3]. Furthermore, a number of medium- to large-size randomized controlled trials (RCTs) (the NOBLE [Nordic-Baltic-British left main revascularization] study [4] and the EXCEL [Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization] trial [5]) and observational studies with propensity-score analysis [6,7] of PCI with DES (DES-PCI) versus CABG for LMCAD have recently reported mid- to long-term results. Propensity-score analysis

Hisato Takagi and Tomo Ando contributed equally to this study.

Meta-Analysis of Circadian Variation in the Onset of Acute Aortic Dissection

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Circadian variation in the onset of acute aortic dissection (AAD) has been less investigated than other cardiovascular diseases. We performed a meta-analysis to assess the presence of an circadian rhythmic variability of AAD onset. Eligible studies were observational studies enrolling patients with AAD and reporting a circadian variation in AAD. Study-specific estimates, that is, 2-hour incidence of AAD, were combined using the random-effects model. Chronobiological analysis (analysis of circadian rhythmicity) was performed by applying a partial Fourier series to the pooled 2-hour incidence using the weighted least-squares method. We identified 7 eligible studies enrolling a total of 1,827 patients with AAD. Pooled 2-hour period incidence of AAD was 3.4% in 0:00 to 2:00, 4.8% in 2:00 to 4:00, 5.4% in 4:00 to 6:00, 9.6% in 6:00 to 8:00, 13.8% in 8:00 to 10:00, 11.1% in 10:00 to 12:00, 8.1% in 12:00 to 14:00, 8.9% in 14:00 to 16:00, 8.8% in 16:00 to 18:00, 7.0% in 18:00 to 20:00, 8.1% in 20:00 to 22:00), and 5.5% in 22:00 to 24:00. Chronobiological analysis (nonlinear Fourier rhythm analysis) identified a significant ($p = 0.0082$) circadian pattern in the occurrence of AAD with a peak in 8:00 to 10:00 and a nadir in 0:00 to 2:00. Pooled analysis demonstrated significantly more incidence in 8:00 to 10:00 than in 0:00 to 2:00 (risk ratio 3.59, 95% confidence interval 2.19 to 5.90, $p < 0.00001$). The incidence of AAD was 8.8%, 15.5%, 25.0%, 17.7%, 16.1%, and 13.8% in 0:00 to 4:00, 4:00 to 8:00, 8:00 to 12:00, 12:00 to 16:00, 16:00 to 20:00, and 20:00 to 24:00, respectively. A significant circadian pattern was found in the occurrence of AAD with a peak in 8:00 to 10:00 and a nadir in 0:00 to 2:00. **(Am J Cardiol 2017;120:1662–1666)**

Circadian rhythms are driven by circadian clocks, which can be defined as a transcriptionally based molecular mechanism based on both positive and negative feedback loops with a free-running period of approximately 24 hours.[1,2] Circadian clocks are identified within almost all mammalian cell types including cardiomyocytes[3] and vascular smooth muscle and endothelial cells,[4] and the onset of various pathologic events such as myocardial infarction and stroke is all time-of-day dependent in humans peaking near the sleep-to-wake transition (i.e., early morning).[1,5] Rhythmic patterns, characterized by a higher risk from 6:00 A.M. to 12:00 P.M., are suggested in the incidence of acute aortic dissection (AAD) or abdominal aortic aneurysm (AAA) rupture.[6] Mechanisms of AAD onset, however, may be distinct from those of AAA rupture.[7,8] In the present article, we performed a meta-analysis to assess the presence of a circadian rhythmic variability of AAD onset.

Methods

All studies investigating the circadian variation in AAD were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through February 2017 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, for elimination of duplicates, and for further analysis. Search terms included "aortic dissection" and "season(s)," "seasonal," "seasonality," "monthly," "weekly," "daily," "circadian," "hourly," "chronology," "chronologic," "chronological," "chronobiology," "chronobiologic" or "chronobiological."

Studies considered for inclusion met the following criteria: the design was an observational study; the study population was patients with AAD; and main outcomes included the circadian variation in AAD. Data regarding the 2-hour incidence of AAD (number of AAD in a 2-hour period divided by that in a day) were abstracted from each individual study. Data were extracted in duplicate by 2 investigators (HT and TA) and independently verified by a third investigator (TU). Disagreements were resolved by consensus.

Study-specific estimates, that is, the 2-hour incidence of AAD, were combined using the random-effects model (1-group meta-analysis). Chronobiological analysis (analysis of circadian rhythmicity) was performed by applying a partial Fourier series to the pooled 2-hour incidence using the weighted

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Meta-Analysis Comparing ≥10-Year Mortality of Off-Pump Versus On-Pump Coronary Artery Bypass Grafting

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Off-pump coronary artery bypass grafting (CABG) is suggested to be associated with an increase in long-term (≥5-year) all-cause mortality. To determine whether off-pump CABG is associated with an increase in very long-term (≥10-year) all-cause mortality, we performed a meta-analysis of propensity-score matched observational comparative studies of off-pump versus on-pump CABG. MEDLINE and EMBASE were searched through May 2017. A hazard ratio of follow-up (including early) all-cause mortality for off-pump versus on-pump CABG was extracted from each individual study. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic hazard ratios in the random-effects model. Of 164 potentially relevant studies, our search identified 16 propensity-score matched observational comparative studies of off-pump versus on-pump CABG with ≥10-year follow-up enrolling a total of 82,316 patients. A pooled analysis of all the 16 studies demonstrated that off-pump CABG was significantly associated with an increase in all-cause mortality (hazard ratio 1.07, 95% confidence interval 1.03 to 1.12, p for effect = 0.0008; p for heterogeneity = 0.30, I^2 = 12%). In a sensitivity analysis, exclusion of any single hazard ratio from the analysis (leave-one-out meta-analysis) did not substantively alter the overall result. There was no evidence of a significant publication bias. In conclusion, off-pump CABG is associated with an increase in very long-term (≥10 years) all-cause mortality compared with on-pump CABG. **(Am J Cardiol 2017;120:1933–1938)**

There is no difference in short-term (30-day) all-cause mortality between off-pump and on-pump coronary artery bypass grafting (CABG).[1–3]Off-pump CABG reduces incidence of postoperative stroke,[1,2] renal dysfunction,[3] mediastinitis,[3] and atrial fibrillation.[1] However, despite these perioperative benefits,[1–3] off-pump CABG is suggested to be associated with an increase in long-term (≥5-year) all-cause mortality.[4] Of available randomized controlled trials of off-pump versus on-pump CABG with ≥5-year follow-up,[5–12] none (with 5–8 years follow-up) has reported very long-term (≥10-year) results. To determine whether off-pump CABG is associated with an increase in ≥10-year all-cause mortality, we performed a meta-analysis of propensity score-matched observational comparative studies of off-pump versus on-pump CABG.

Methods

All propensity-score matched observational comparative studies of off-pump versus on-pump CABG with very long-term (≥10-year) follow-up were identified using a 2-level search strategy. First, databases including MEDLINE and EMBASE were searched through May 2017 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 *off-pump*, and *propensity*, and *matching* or *matched*.

Studies considered for inclusion met the following criteria: the design was a propensity score-matched observational comparative study; the study population comprised patients undergoing CABG; patients were assigned to off-pump versus on-pump CABG; and main outcomes included ≥10-year all-cause mortality. A hazard ratio with its 95% confidence interval (CI) of follow-up (including early) all-cause mortality for off-pump versus on-pump CABG was extracted from each individual study. For studies not reporting a hazard ratio with corresponding variance, this was calculated from Kaplan-Meier curve or summary data using a hazard-ratio calculations spreadsheet provided by Tierney et al[13] based on statistical methods reported by Parmar et al[14] and Williamson et al.[15] Data were extracted in duplicate by 2 investigators (HT, TA) and independently verified by a third investigator (TU). Disagreements were resolved by consensus.

Study-specific estimates were combined using inverse variance-weighted averages of logarithmic hazard ratios in the random-effects model. Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual studies one at a time and

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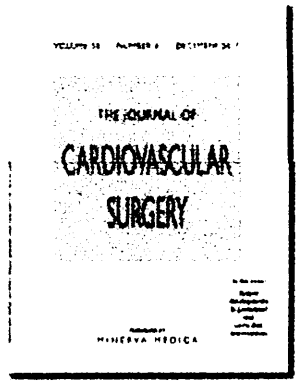

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Meta-analysis of day-of-week variation of acute aortic rupture or dissection

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BACKGROUND: We performed a meta-analysis to assess the presence of a day-of-week rhythmic variability of acute aortic rupture or dissection (AARD) onset.
METHODS: Eligible studies were observational studies enrolling patients with AARD and reporting day-of-week variation of AARD. Study-specific estimates, i.e. day-of-week incidence of AARD, were combined using the random-effects model. Chronobiological analysis was performed by applying a partial Fourier series to pooled day-of-week incidence by using the inverse-variance weighted least-squares method.
RESULTS: We identified 9 eligible studies enrolling a total of 28,036 patients with AARD. Pooled incidence of AARD was 12.8% on Sunday, 15.9% on Monday, 14.8% on Tuesday, 15.1% on Wednesday, 14.7% on Thursday, 14.1% on Friday, and 12.1% on Saturday. Chronobiological analysis identified a significant (P = 0.0098) day-of-week in the occurrence of AARD with a peak on Monday and a nadir on Saturday. Pooled analysis demonstrated significantly more incidence on Monday than on Saturday (relative risk, 1.247; 95% confidence interval, 1.131 to 1.374; P = 0.012).
CONCLUSIONS: Incidence of AARD was 12.8%, 15.9%, 14.8%, 15.1%, 14.7%, 14.1%, and 12.1%, on Sunday, Monday, Tuesday, Wednesday, Thursday, Friday, and Saturday, respectively. A significant day-of-week pattern in the occurrence of AARD with a peak on Monday and a nadir on Saturday was identified with significantly more incidence on Monday than on Saturday.

KEY WORDS: Acute aortic rupture or dissection - Day-of-week variation - Meta-analysis

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ORIGINAL STUDIES

WILEY

Long-term survival after transcatheter versus surgical aortic valve replacement for aortic stenosis: A meta-analysis of observational comparative studies with a propensity-score analysis

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Abstract

Objectives: To synthesize evidence regarding long-term survival after transcatheter aortic valve implantation (TAVI) versus surgical aortic valve replacement (SAVR) for severe aortic stenosis (AS) from real-world clinical practice, we performed a meta-analysis of observational studies with a propensity-score analysis and ≥3-year follow-up.

Methods: Databases including MEDLINE and EMBASE were searched through April 2017 using PubMed and OVID. Eligible studies were observational comparative studies with a propensity-score analysis of TAVI versus SAVR enrolling patients with severe AS and reporting ≥3-year all-cause mortality as an outcome. A hazard ratio (HR) with its 95% confidence interval (CI) of follow-up (including early) mortality for TAVI versus SAVR was extracted from each individual study.

Results: Our search identified 14 eligible studies enrolling a total of 4,197 patients. A pooled analysis of all the 14 studies demonstrated a statistically significant 54% increase in mortality with TAVI relative to SAVR (HR, 1.54; 95% CI, 1.31–1.81; P for effect < 0.00001; P for heterogeneity = 0.14; I^2 = 30%). Several sensitivity analyses did not substantially change the statistically significant benefit for SAVR. There was no evidence of significant publication bias.

Conclusions: On the basis of a meta-analysis of 14 observational comparative studies with a propensity-score analysis including a total of ≥4,000 patients, TAVI is associated with worse ≥3-year overall survival than SAVR.

KEYWORDS

aortic stenosis, long-term survival, meta-analysis, propensity-score analysis, surgical aortic valve replacement, transcathter aortic valve implantation

1 | INTRODUCTION

To the best of our knowledge, five randomized controlled trials (RCTs) (Placement of Aortic Transcatheter Valves [PARTNER] 1 [1], PARTNER 2 [2], CoreValve US Pivotal [3], Nordic Aortic Valve Intervention [NOTION] [4], and Surgical Replacement and Transcatheter Aortic Valve Implantation [SURTAVI] [5]) of transcatheter aortic valve implantation (TAVI) versus surgical aortic valve replacement (SAVR) for severe aortic stenosis (AS) reported ≥2-year all-cause mortality. Although there is no statistically significant difference in follow-up mortality between TAVI and SAVR in all the five RCTs [1–5], ≥3-year mortality is available in only two RCTs (PARTNER 1 [1] with 5-year follow-up and CoreValve US Pivotal [3] with 3-year follow-up). Furthermore, patients enrolled in RCTs may not be representative of those typically seen in real-world clinical practice. Indeed, approximate 80% (77.5% in

Hisato Takagi and Shohei Mitta contributed equally to this study and share the first authorship.

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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Editorial

The lion and the unicorn were fighting for the crown: on-pump versus off-pump coronary-artery bypass grafting

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"..., *in the middle of which the Lion and Unicorn were fighting.*

..., *that at first Alice could not make out which was which: but she soon managed to distinguish the Unicorn by his horn.*"

Numerous studies [including randomized controlled trials (RCTs)] have compared outcomes following off-pump coronary-artery bypass grafting (CABG) with those following on-pump CABG, which appears that, as it were, "the Lion and the Unicorn were fighting for the crown" (*Figure 1*). Recently, the Randomized On/Off Bypass (ROOBY) Follow-up Study (ROOBY-FS) (1) reported 5-year clinical outcomes in 2,203 patients randomly assigned to off-pump (1,104 patients) or on-pump CABG (1,099 patients). At 5 years, off-pump CABG was inferior to on-pump CABG with regard to death from any cause [15.2% *vs.* 11.9%; relative risk (RR), 1.28; 95% confidence interval (CI), 1.03–1.58; P=0.02; hazard ratio (HR), 1.30; 95% CI, 1.04–1.64; P=0.02] and the primary composite major adverse cardiovascular events outcome (RR, 1.14; 95% CI, 1.00–1.30; P=0.046; HR, 1.18; 95% CI, 1.01–1.38; P=0.03). Has the Lion (on-pump CABG) beaten the Union (off-pump CABG)?

The 5-year rate of death from cardiac causes did not differ significantly between off- and on-pump CABG (6.3% *vs.* 5.3%; RR, 1.20; 95% CI, 0.86–1.68; P=0.29) in the ROOBY-FS (1). Accordingly, the significantly higher rate of death from any cause following off-pump (15.2%) than on-pump CABG (11.9%) was not correspondingly reflected in no significantly different rate of death from cardiac causes between treatments. The discrepancy between the significant difference of all-cause mortality and no difference of cardiac mortality in the ROOBY-FS (1) is in accordance with 5-year results of another RCT, i.e., the Best Bypass Surgery (BBS) trial (2). In the BBS trial (2), although all-cause mortality was significantly higher following off-pump than on-pump CABG (HR, 1.66; 95% CI, 1.02–2.73; P=0.04), cardiac mortality was similar between off-pump and on-pump CABG (10% *vs.* 7 %; HR, 1.30; 95% CI, 0.64–2.66; P=0.47) (2). Because the cause of death may have several competitive factors in high-risk patients and death from cardiac causes is always challenging to adjudicate, the reliability of assessing cardiac causes of death has been much debated and all-cause mortality must be the most unbiased outcome (1,2).

A number of meta-analyses (3-5) have confirmed the results of the ROOBY-FS (1). A meta-analysis (3) demonstrated that off-pump CABG increased short-term (≥1-year) [18 RCTs enrolling a total of 5,358 patients; pooled odds ratio (OR), 1.35; 95% CI, 1.07–1.70; P=0.01] and midterm (≥3-year) all-cause mortality (7 RCTs enrolling a total of 1,826 patients; pooled OR, 1.36; 95%

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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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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

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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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. (Am J Cardiol 2017;119:1250–1254)

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 1252 for disclosure information.

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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) are 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 mellitus, and peripheral vascular disease (PVD) patients. Patients who underwent TAVR from 2011 to 2014 in the United States were identified using the International Classification of Diseases-Ninth Revision code 35.05 from the Nationwide Inpatient Sample database. Frequency of any VC (per 100 transcatheter aortic valve implantation procedure or hospital discharges) for each year from 2011 to 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 was 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 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. (Am J Cardiol 2017;119:1433–1437)

Transcatheter aortic valve replacement (TAVR) has dramatically changed the management of severe symptomatic aortic stenosis. However, certain perioperative complications occur at higher rates compared with surgical aortic valve replacement including vascular complication (VC).[1,2] VC has been reported to be associated with worse outcomes after TAVR.[3,4] According to data from The Society of Thoracic Surgeons/American College of Cardiology annual outcomes, VC rates have trended down from 5.6% in 2012 to 2013 to 4.2% in 2014.[5] However, it is unclear whether VC has decreased in patients who are at elevated risk such as female gender,[6–10] diabetes mellitus (DM),[8,11] peripheral vascular disease (PVD), and femoral arterial calcification.[12,13] Accordingly, the purpose of the present study is to assess the trends of VC incidence, particularly in high-risk subgroups using the nationwide inpatient sample (NIS) data.

Methods

This study was conducted using the NIS of the Health Care Utilization Project. Details of the design and description of the NIS is available online (*https://www.hcup-us.ahrq.gov/*).

The present study utilizes information on adult patients (age ≥ 18 years) who underwent TAVR across the country between 2011 and 2014. Only patients who underwent transfemoral or transaortic replacement were included in this study. These were identified using International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM) procedure code 35.05.

Data on patient and hospital-level characteristics were provided for each patient in the NIS. However, identifiable variables were not included to preserve both patient and hospital privacies. Patient-level factors including demographics, diagnoses, co-morbidities, in-hospital procedures, disposition, and so on, as well as hospital-level

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Transfemoral, transapical and transcatheter aortic valve implantation and surgical aortic valve replacement: a meta-analysis of direct and adjusted indirect comparisons of early and mid-term deaths

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Summary

Clinical outcomes of transfemoral-transcatheter aortic valve implantation (TF-TAVI) versus surgical aortic valve replacement (SAVR) or transapical (TA)-TAVI are limited to a few randomized clinical trials (RCTs). Because previous meta-analyses only included a limited number of adjusted studies or several non-adjusted studies, our goal was to compare and summarize the outcomes of TF-TAVI vs SAVR and TF-TAVI vs TA-TAVI exclusively with the RCT and propensity-matched cohort studies with direct and adjusted indirect comparisons to reach more precise conclusions. We hypothesized that TF-TAVI would offer surgical candidates a better outcome compared with SAVR and TA-TAVI because of its potential for fewer myocardial injuries. A literature search was conducted through PUBMED and EMBASE through June 2016. Only RCTs and propensity-matched cohort studies were included. A direct meta-analysis of TF-TAVI vs SAVR, TA-TAVI vs SAVR and TF-TAVI vs TA-TAVI was conducted. Then, the effect size of an indirect meta-analysis was calculated from the direct meta-analysis. The effect sizes of direct and indirect meta-analyses were then combined. A random-effects model was used to calculate the hazards ratio and the odds ratio with 95% confidence intervals. Early (in-hospital or 30 days) and mid-term (≥1 year) all-cause mortality rates were assessed. Our search resulted in 4 RCTs ($n = 2319$) and 14 propensity-matched cohort ($n = 7217$) studies with 9536 patients of whom 3471, 1769 and 4296 received TF, TA and SAVR, respectively. Direct meta-analyses and combined direct and indirect meta-analyses of early and mid-term deaths with TF-TAVI and SAVR were similar. Early deaths with TF-TAVI vs TA-TAVI were comparable in direct meta-analyses (odds ratio 0.64, $P = 0.35$) and direct and indirect meta-analyses combined (odds ratio 0.73, $P = 0.24$). Mid-term deaths with TF-TAVI vs TA-TAVI were increased (hazard ratio 0.83, $P = 0.07$) in a direct meta-analysis and became significant after addition of the indirect meta-analysis (hazard ratio 0.78, 95% confidence interval 0.67-0.92, $P = 0.003$). In conclusion, TF-TAVI was associated with similar early and mid-term deaths compared with SAVR. The number of early deaths was not significantly different between TF-TAVI and TA-TAVI; whereas there were fewer mid-term deaths with TF-TAVI than with TA-TAVI.

Keywords: Transcatheter aortic valve implantation • Transfemoral • Transapical

INTRODUCTION

Recent advancements in device technologies (i.e. reduction in sheath size) have allowed transcatheter aortic valve implantation (TAVI) to be performed more frequently using the transfemoral (TF) approach, which is the preferred approach. However, not all patients are able to undergo TF-TAVI, mainly because of heavy calcification, tortuosity or small size of the femoral artery. Therefore, the transapical (TA) approach is performed in a non-negligible proportion of patients [1].

It is speculated that the numbers of TF-TAVI procedures will increase with the availability of the newer generations of prosthetic valves and delivery devices. Several studies have suggested that TA-TAVI has worse outcomes compared with SAVR [2, 3]. However, few data are available to compare clinical outcomes with TF-TAVI and with surgical aortic valve replacement (SAVR). TF-TAVI is the most utilized approach and considered the preferred approach because it is less invasive [1]. Therefore, it is paramount to compare the clinical outcomes of TF-TAVI and SAVR. In addition, it is important to shed more light on the clinical outcomes of TF-TAVI versus TA-TAVI, as the number of TF-TAVI procedures increases.

Past studies have assessed TF-TAVI versus SAVR and TF-TAVI versus TA-TAVI [4-7]. However, previous meta-analyses of TF-TAVI versus SAVR comprised only 4 studies that did not include all TF-TAVI patients [4, 5]. Hence, statistical power may have been limited. Previous meta-analyses of TF-TAVI versus TA-TAVI were meta-analyses of non-randomized studies or were meta-

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Original article

Does diabetes mellitus impact prognosis after transcatheter aortic valve implantation? Insights from a meta-analysis

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ABSTRACT

Background: Diabetes mellitus (DM) is well known to increase mortality in several cardiovascular diseases. However, the prognostic impact of DM following transcatheter aortic valve implantation (TAVI) remains controversial. We sought to assess the impact of DM on perioperative (in-hospital or 30-day) complications and mid-term (≥1 year) all-cause mortality after TAVI through meta-analysis.

Methods: A comprehensive literature search of PUBMED and EMBASE was conducted through January 1st 2002 to May 15th 2016. Articles that reported adjusted hazards ratio (HRs) or unadjusted HR for mid-term all-cause mortality with 95% confidence intervals (CIs) of DM or insulin dependent DM (IDDM) on mid-term all-cause mortality post TAVI were included in the analysis. A meta-analysis was performed with combination of both adjusted HR and un-adjusted HR. Sensitivity analysis was performed with only the adjusted HR. Random-effects model was used to calculate the pooled effect size.

Results: A total of 22 observational cohort studies were identified with 28,440 (8998 DM and 19,442 non-DM) patients. The risk of perioperative complications (myocardial infarction, bleeding, major vascular complications, stroke, and new-onset atrial fibrillation) was similar between DM and non-DM cohorts. A meta-analysis of all-cause mortality of DM (19 studies after excluding 3 studies that only reported HR of IDDM on mid-term all-cause mortality, 8808 DM and 17,829 non-DM patients) resulted in significantly worse outcome (HR 1.21, 95%CI 1.10–1.34, $p = 0.0002$, $I^2 = 53\%$) in DM patients compared to non-DM patients post-TAVI. Sensitivity analysis showed consistent results. Subgroup analysis (4 studies with 267 IDDM versus 2161 non-IDDM) demonstrated that IDDM was associated with higher all-cause mortality (HR 2.05, 95%CI 1.54–2.73, $p < 0.00001$, $I^2 = 0\%$) following TAVI.

Conclusions: DM was associated with similar perioperative complications but was associated with increased mid-term all-cause mortality after TAVI. Further study of the causes of increased mortality during the follow-up may lead to improved outcome.

Introduction

Diabetes mellitus (DM) is a major public health issue, which affects more than 400 million people and is expected to surpass 600 million by 2040 worldwide [1]. DM accounted for 15% of mortality and its burden on mortality nearly doubled in the past few decades [2]. DM has been reported to be associated with increased mortality in a wide variety of cardiovascular diseases [3–5].

Transcatheter aortic valve implantation (TAVI) has initially emerged as a viable option for the treatment of severe symptomatic aortic stenosis (AS) in inoperable and high-risk patients for open-heart surgery [6,7]. Recently, those at intermediate risk for surgery also exhibited similar clinical outcomes [8]. The number of TAVI procedures has been increasing exponentially and is expected to continue to rise considering that it demonstrated comparable outcomes with surgical aortic valve replacement (SAVR) at intermediate surgical risk [8–10].

DM in TAVI candidates is one of the most common comorbidities, reaching approximately 30% of the entire cohort [7,8]. Although DM is an established risk factor for increased morality in certain cardiovascular diseases (i.e. coronary artery disease), its

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Complete versus incomplete revascularization with drug-eluting stents for multi-vessel disease in stable, unstable angina or non-ST-segment elevation myocardial infarction: A meta-analysis

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Objectives: To determine whether drug-eluting stent (DES) coronary complete revascularization (CR) confers clinical benefit over incomplete revascularization (IR) in patients with multivessel coronary artery disease (MVD).

Background: Clinical benefit of CR over IR in patients with MVD with angina (both stable and unstable) and non-ST-segment elevation myocardial infarction (NSTEMI) in DES has not been well studied.

Methods: We conducted a systematic online literature search of PUBMED and EMBASE. Literatures that compared the clinical outcomes between CR and IR with exclusively or majority (>80%) using DES in patients without or included only small portion (<20%) of ST-segment elevation myocardial infarction or single-vessel coronary artery disease were included. Hazards ratio (HR) with 95% confidence interval (CI) was calculated with random-effects model.

Results: No randomized clinical trials were identified. A total of 14 observational studies with total of 41 687 patients (CR 39.6% and IR 60.4%) were included in this meta-analysis. CR was associated with lower incident of all-cause mortality (HR 0.71, $P = 0.001$), major adverse events (HR 0.75, $P < 0.001$), cardiovascular mortality (HR 0.39, $P < 0.001$). Meta-regression analysis showed that CR significantly reduced the risk of all-cause mortality in advanced age, triple vessel disease and male sub-groups.

Conclusions: CR with DES conferred favorable outcomes compared to IR in MVD patients with stable, unstable angina or NTEMI. Further research to achieve higher CR in MVD patients may lead to improvement in prognosis in these cohorts.

KEYWORDS
drug-eluting stents, multi-vessel coronary artery disease, revascularization

1 | INTRODUCTION

Multi-vessel coronary artery disease (MVD) is relatively common in coronary artery disease and poses challenges to revascularization strategy. Complete revascularization (CR) versus incomplete revascularization (IR) in MVD with percutaneous coronary intervention (PCI) has been investigated in several studies for various form of coronary artery disease.[1,2] The outcomes were in favor of CR in ST-segment elevation myocardial infarction (STEMI) with MVD.[3,4] Previous studies have investigated the benefit of CR versus IR in patients without STEMI and MVD. Zimarino et al reported in their meta-analysis that CR was also associated with

Tomo Ando and Hisato Takagi contributed equally to this work.

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Cardiovascular Revascularization Medicine

Comparison of outcomes in new-generation versus early-generation heart valve in transcatheter aortic valve implantation: A systematic review and meta-analysis☆,☆☆

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ABSTRACT

Background: New-generation (NG) valves for transcatheter aortic valve implantation (TAVI) has recently been widely used in real-world practice, yet its comparative outcomes with early-generation (EG) valves remain under-explored.

Methods: An electronic literature search using PUBMED and EMBASE was conducted from inception to April 2017 for matched-cohort studies. Articles that compared the outcomes of NG vs. EG valves post TAVI with at least one of the following clinical outcome reported were included: all-cause mortality, major or life-threatening bleeding, major vascular complications (MVC), significant (more than moderate) paravalvular regurgitation (PVR), cerebrovascular events, significant (stage 2 or 3) acute kidney injury (AKI) and new permanent pacemaker implantation (PPI) that occurred either in-hospital or within 30-days.

Results: A total of 6 observational matched-cohort studies with 585 and 647 patients included in NG and EG valves, respectively, were included. EG valves were associated with a lower incidence of major or life-threatening bleeding (5.7% vs. 15.7%, $p < 0.00001$), significant paravalvular regurgitation (5.3% vs. 14.4%, $p = 0.001$), and significant AKI (4.4% vs. 7.5, $p = 0.03$). All-cause mortality (3.5% vs. 5.0, $p = 0.43$), cerebrovascular events (3.4% vs. 2.3%, $p = 0.34$) and new PPI (11.0% vs. 14.6%, $p = 0.52$) were similar between the two groups. NG demonstrated lower tendency of MVC (2.5% vs. 7.2, $p = 0.09$) compared to EG valves.

Conclusions: NG demonstrated lower rates of significant AKI, significant PVR and major or life-threatening bleeding while all-cause mortality, new PPI, and cerebrovascular events remained similar compared to EG valves.

1. Introduction

Several randomized control trials have shown non-inferior clinical outcomes of transcatheter aortic valve implantation (TAVI) compared to surgical aortic valve replacement for the treatment of symptomatic, severe aortic stenosis at high and intermediate surgical risk patients [1,2]. These trials have mainly deployed early-generation (EG) valves (Sapien, Sapien XT or CoreValve). Certain perioperative complications, especially vascular complications and paravalvular regurgitation (PVR) occurred more in TAVI compared to surgical aortic valve replacement and therefore, several new-generation (NG) valves have been developed to overcome these issues. So far, NG valves have demonstrated its promising clinical outcomes in several registries [3–5].

Studies that compared outcomes of NG vs. EG valve have shown lower rates of vascular complication and PVR while other complications such as stroke, new pacemaker implantation, and bleeding remained similar in certain studies [6–9]. The previous meta-analysis pooled the performance of NG valves but did not compare the outcomes with the EG valves and therefore, although the perioperative complications were overall low, the performance of NG valve remained unclear compared to EG valves [10]. It is imperative to explore the comparative outcomes of NG vs. EG valves to identify the clinical outcomes where NG and EG perform similarly in order to aid future research by suggesting areas of improvement.

Abbreviations: AKI, acute kidney injury; CI, confidence interval; EG, early-generation; MVC, major vascular complication; NG, new-generation; OR, odds ratio; PVR, paravalvular regurgitation; PPI, permanent pacemaker implantation; TAVI, transcatheter aortic valve intervention.

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Comparison of In-Hospital Outcomes of Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement in Obese (Body Mass Index ≥ 30 Kg/M2) Patients

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The comparative outcomes of transcatheter aortic valve implantation (TAVI) versus surgical aortic valve replacement (SAVR) in obese (body mass index ≥ 30 kg/m^2) patients are underexplored. Nationwide Inpatient Sample database was queried from 2011 to 2014, and those who underwent TAVI or SAVR with obesity were identified. A complete case analysis with multivariate analysis was performed to adjust for the difference in underlying co-morbidities. We identified a total of 12,525 patients (989 TAVI and 11,536 SAVR). TAVI patients were elderly, more women, and had higher co-morbidity burden represented by a higher Deyo's modification of Charlson's score. Inpatient mortality was similar between the 2 groups (2.6% vs 3.2%, p = 0.21). TAVI patients had less hemorrhage requiring transfusion (8.5% vs 18%, p < 0.01), cardiac complication (7.3% vs 14%, p < 0.01), respiratory complication (1.3% vs 3.9%, p < 0.01), postop sepsis (1.0% vs 3.2%, p < 0.01), acute myocardial infarction (2.5% vs 5.5%, p < 0.01), acute kidney injury (18% vs 22%, p < 0.001), and nonroutine discharge (62% vs 67%, p < 0.001). Conversely, vascular complication (5.6% vs 4.5%, p = 0.04), new pacemaker (13% vs 5.4%, p < 0.001), and use of extracorporeal oxygen membrane (1.1% vs 0.3%, p = 0.002) were observed more frequently in TAVI patients. The median hospital cost was higher in TAVI ($50,957 vs $44,977, p = 0.004), whereas TAVI patients had a significantly shorter hospital stay (median 7.4 vs 10 days, p < 0.001). TAVI portended similar in-hospital mortality and less certain perioperative complications. In TAVI, the medical cost was higher, but the length of stay was shorter and nonroutine discharge was less frequent. © 2017 Elsevier Inc. All rights reserved. **(Am J Cardiol 2017;120:1858–1862)**

The purpose of this study was to examine the prevalence of obesity in patients who underwent transcatheter aortic valve implantation (TAVI) in the United States and to compare the in-hospital outcomes in TAVI versus surgical aortic valve replacement (SAVR) in obese (body mass index [BMI] ≥ 30 kg/m^2) patients using the Nationwide Inpatient Sample (NIS) database.

Methods

This study was conducted using data from the NIS of the Health Care Utilization Project sponsored by the Agency for Healthcare Research and Quality. Details of the design and description of the NIS is available online (*https://www.hcup-us.ahrq.gov/nisoverview.jsp*). In brief, the NIS is a stratified sampling of hospital 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 per year. The patient population involved in this study are adult obese patients who underwent a TAVI or SAVR procedure in the United States between 2011 and 2014. Obese patients were defined as those with BMI ≥ 30 and identified with International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM) codes 278.00 and 278.01. TAVI cases were identified by ICD-9-CM procedure code 35.05, whereas SAVR cases were identified using ICD-9-CM procedure codes 35.21 and 35.22. Data on patient-level factors including demographics, diagnoses, co-morbidities, in-hospital procedures, and disposition, as well as hospital-level factors including bed size, location, and total number of hospitalizations, were available via the NIS database.

Our primary end point was in-hospital mortality defined as death at any time during the index hospitalization. In addition, we evaluated periprocedural complications including hemorrhage requiring transfusion, cardiac complication, vascular complication, neurologic complication, respiratory

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See page 1861 for disclosure information.

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ORIGINAL STUDIES

A systematic review of reported cases of combined transcatheter aortic and mitral valve interventions

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Abstract

Objectives: To summarize the published data of combined transcatheter aortic and mitral valve intervention (CTAMVI).

Background: CTAMVI, a combination of either transcatheter aortic valve replacement (TAVR) or transcatheter aortic valve-in-valve (TAViV) and transcatheter mitral valve replacement (TMVR), transcatheter mitral valve-in-valve/valve-in-ring (TMViV/ViR), or percutaneous mitral valve repair (PMVR) is an attractive alternative in high-surgical risk patients with combined aortic and mitral valve disease. However, its procedural details and clinical outcomes have not been well described.

Methods: We performed a systematic review of all the published articles from PUBMED and EMBASE.

Results: A total of 37 studies with 60 patients were included. The indication for CTAMVI was high or inoperable surgical risk and symptomatic severe aortic stenosis (92%) or severe aortic regurgitation (8%) combined with moderate to severe/severe mitral stenosis (30%) or moderate/severe mitral regurgitation (65%) or both (5%). In majority of the cases, aortic valve intervention was performed prior to the mitral valve. Mortality rate were 25% for TAVR + TMVR (range 42 days to 10 months), 17% for TAVR + TMViV/ViR (range 13 days to 6 months), 0% for TAViV + TMViV/ViR (range 6–365 days), and 15% for TAVR/ViV + PMVR (range 17 days to 419 days). Significant (more than moderate) paravalvular regurgitation post-procedure was rare.

Conclusions: CTAMVI appears to confer reasonable clinical outcome. Further large study is warranted to clarify the optimal strategy, procedural details and clinical outcomes in the future.

KEYWORDS

mitraclip, transcatheter aortic valve replacement, transcatheter mitral valve repair, valve-in-valve

1 | INTRODUCTION

Surgical repair or replacement remains the gold standard for severe valvular heart disease. However, recent innovations in transcatheter valve therapy, especially for aortic and mitral valve with the transcatheter aortic valve replacement (TAVR), transcatheter mitral valve replacement (TMVR), and percutaneous mitral valve repair (PMVR), have allowed the treatment of patients deemed at high-risk or inoperable for open-heart surgery for severe symptomatic aortic stenosis, mitral regurgitation (MR) and mitral stenosis [1–4]. In addition, transcatheter aortic valve-in-valve (TAViV) and transcatheter mitral valve-in-valve/valve-in-ring (TMViV/ViR) therapy has enabled clinicians to treat severe stenosis or insufficiency caused by deterioration of previously replaced bioprosthetic valve [5–7].

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Single versus dual anti-platelet therapy post transcatheter aortic valve implantation: a meta-analysis of randomized controlled trials

Tomo Ando[1,4] · Hisato Takagi[2] · Alexandros Briasoulis[3] · Luis Afonso[1]

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Abstract The purpose of this systematic review and meta-analysis was to assess the 30-days safety (bleeding and vascular events) and efficacy (reduction in major stroke, myocardial infarction and mortality) of single anti-platelet (SAPT) versus dual anti-platelet (DAPT) after transcatheter aortic valve implantation (TAVI). We used a meta-analytic method with Mantel–Haenszel methods to calculate the odds ratio (OR) and 95% confidence interval (CI). Only randomized clinical trials that compared 30-days safety and efficacy based on Valve Academic Research Consortium criteria were included. Studies that included patients on anticoagulants were excluded. Our analysis included three studies with a total of 421 patients (210 SAPT and 211 DAPT). Life-threatening and major bleeding as well as major vascular complications was similar between SAPT and DAPT. Similarly, major stroke, myocardial infarction and mortality was also comparable between the two groups. The combined outcomes of 30-day mortality, life-threatening and major bleeding showed tendency toward lower event rates in SAPT compared to DAPT (9.5 vs. 15.6%, OR 0.57; 95% CI 0.31–1.03, p = 0.06). In conclusion, SAPT provided similar safety without adding incremental efficacy compared to DAPT but showed tendency of lower combined endpoints of 30-day mortality, life-threatening and major bleeding.

Keywords Transcatheter aortic valve implantation · Single antiplatelet therapy · Dual antiplatelet therapy

Introduction

Transcatheter aortic valve implantation (TAVI) has demonstrated similar mid to long-term mortality compared to surgical aortic valve replacement for symptomatic, severe aortic stenosis [1, 2]. One of the major areas that remain controversial in care of patients who have undergone TAVI is the optimal regimen and duration of anti-platelet therapy. Current guideline recommends dual anti-platelet (DAPT) for 6 months over single anti-platelet (SAPT) therapy, however, this is based only on expert opinion [3]. Although anti-platelet therapy is considered necessary to avoid valve related events until appropriate endothelialization is achieved, TAVI patients often have multiple comorbidities that may expose them at increased risk of bleeding or atherosclerosis related events (i.e. stroke, myocardial infarction), which makes it difficult to balance the risk and benefit of anti-platelet regimen and duration. It is of paramount importance to explore the safety and efficacy of SAPT and DAPT following TAVI to adjust the risk and benefit of bleeding and atherosclerosis related events.

Several previous studies and meta-analyses have addressed this topic. Nonetheless, individual randomized controlled studies have been unable to draw conclusions because of low cohort numbers, while results of other

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ORIGINAL STUDIES

WILEY

Does mild paravalvular regurgitation post transcatheter aortic valve implantation affect survival? A meta-analysis

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Abstract

Background: To assess the impact of post transcatheter aortic valve implantation (TAVI) mild paravalvular regurgitation (PVR) on mortality. More than moderate PVR after TAVI has decreased with the advent of new-generation prosthetic valves. However, mild PVR remains common and its clinical impact has been inconsistent. We aimed to assess the impact of mild PVR through meta-analysis.

Methods and Results: A systematic literature search was conducted through PUBMED and EMBSE. Manuscripts that reported hazard ratio (HR) with 95% confidence interval (CI) for clinical outcome of interest (all-cause and cardiac mortality) has been included. Random-effects model was used for calculation of HR. A total of 25 articles including total of 21,018 patients were finally included for quantitative synthesis (meta-analysis). Our pooled analysis demonstrated higher all-cause mortality in patients with mild PVR compared to none/trivial PVR (HR 1.26, 95%CI 1.11-1.43, I^2=45%, $p < 0.001$) (follow up duration range 6 months to 5 years). Significant heterogeneity among studies was observed (p for heterogeneity = 0.005). Egger's test showed no evidence of publication bias. Cardiovascular mortality was increased in patients with mild PVR compared with none/trivial PVR (HR 1.28, 95%CI 1.05-1.57, I^2=8%, $p = 0.02$) (follow up duration range 1-3 years).

Conclusions: Mild PVR was associated with increased all-cause and cardiovascular mortality after TAVI. Whether further interventions in mild PVR is of benefit, has yet to be determined.

KEYWORDS

aortic valve disease, meta-analysis, transcatheter valve implantation

1 | INTRODUCTION

Paravalvular regurgitation (PVR) after transcatheter aortic valve implantation (TAVI) is fairly common. More than moderate PVR was associated with increased mid-term all-cause mortality [1]. With the advent of newer-generation prosthetic valves, the incidence of more than moderate PVR has declined dramatically [2]. However, the rate of mild PVR remains relatively high even with the new-generation prosthetic valves [3,4] and the impact of mild PVR compared to none/trivial PVR on clinical outcome has not been well studied. Mild PVR was associated with worse outcomes in some [5,6] but not all [7-9] studies. A previous meta-analysis by Athappan and colleagues reported that mild PVR was associated with worse mortality [10]. However, only five studies were included and the result was inconsistent when sensitivity analysis was performed.

Since mild PVR remains highly prevalent even when newer-generation prosthetics are implanted, it is clinically important to assess its impact on mortality. TAVI has demonstrated similar all-cause mortality and disabling stroke compared with surgical aortic valve replacement in intermediate risk category and further assessment of the

Abbreviations: CI, confidence interval; HR, hazard ratio; TAVI, transcatheter aortic valve implantation; PARTNER, placement of aortic transcatheter valves; PVR, paravalvular regurgitation.

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ORIGINAL STUDIES

WILEY

Hospital outcomes of transcatheter versus surgical aortic valve replacement in female in the United States

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Abstract

Objectives: To assess the in-hospital mortality and complications in female between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

Background: Female is one of the risk factors for increased adverse events in cardiac surgery.

Methods and results: Nationwide Inpatient Sample database was queried from 2011 to 2014 for patients who underwent TAVR or SAVR in female patients. The primary endpoint was in-hospital all-cause mortality and second endpoints were perioperative complications. We performed a propensity score analysis to calculate the adjusted odds ratio (OR) for each outcome. Patients who had concomitant cardiac surgery and those who had TAVR or SAVR mainly for aortic regurgitation were excluded. Our query from 2011 to 2014 resulted in a total of 3,067 TAVR and 18,594 SAVR in female patients. TAVR patients were in general elder and had a higher burden of comorbidities. The primary endpoint was similar between TAVR and SAVR (4.2% vs. 3.9%, OR 1.0, $P = 0.89$). Compared to SAVR, female TAVR patients had less hemorrhage requiring transfusion (12% vs. 21%, OR 0.41, $P < 0.001$), perioperative cardiac arrest and nonfatal myocardial infarction (9.8% vs. 17%, OR 0.38, $P < 0.001$), respiratory complication (1.6% vs. 4.4%, OR 0.28, $P < 0.001$), post-op sepsis (1.7% vs. 2.9%, OR 0.65, $P = 0.03$), acute myocardial infarction (3.0% vs. 4.9%, OR 0.60, $P < 0.001$), and acute kidney injury (15% vs. 18%, OR 0.62, $P < 0.001$). Conversely, female TAVR patients had significantly increased risk of new pacemaker implantation (11% vs. 5.9%, OR 1.7, $P < 0.001$) and use of extracorporeal membrane oxygenation (0.66% vs. 0.24%, OR 2.8, $P < 0.001$). TAVR patients had less nonroutine discharge. The median hospital cost was significantly higher in TAVR than SAVR (median $51,274 vs. $43,677, $P < 0.001$) but the length of stay was shorter (mean 7.8 days vs. 10.5 days).

Conclusions: TAVR may be a better option for those patients with underlying comorbidities that predispose them at higher risk for complications that was less observed in TAVR group. However, higher cost and increased risk of need for extracorporeal membrane oxygenation, although rare, should be taken into consideration upon deciding the optimal mode for aortic valve replacement.

KEYWORDS

aortic stenosis, female, surgical aortic valve replacement, transcatheter aortic valve replacement, women

Meta-Analysis Comparing Patent Foramen Ovale Closure Versus Medical Therapy to Prevent Recurrent Cryptogenic Stroke

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New evidence suggests that closure of a patent foramen ovale (PFO) plus medical therapy (MT; antiplatelet or anticoagulation) is superior to MT alone to prevent recurrent cryptogenic stroke. We performed a meta-analysis of randomized controlled trials that compared PFO closure plus MT with MT alone in patients with cryptogenic stroke. The efficacy end points were recurrent stroke, transient ischemia attack, and death. The safety end points were major bleeding and newly detected atrial fibrillation. Trials were pooled using random effects and fixed effects models. A trial sequential analysis was performed to assess if the current evidence is sufficient. Risk ratios (RR) were calculated for pooled estimates of risk. Five randomized controlled trials (3,440 patients) were included. Mean follow-up was 4.1 years. PFO closure reduced the risk of recurrent stroke by 58% (RR 0.42, 95% CI 0.20 to 0.91, p = 0.03). The number needed to treat was 38. The cumulative Z-line crossed the trial sequential boundary, suggesting there is adequate evidence to conclude that PFO closure reduces the risk of recurrent stroke by 60%. PFO closure did not reduce the risk of transient ischemia attack (RR 0.78, 95% CI 0.53 to 1.15, p = 0.21), mortality (RR 0.74, 95% CI 0.35 to 1.60, p = 0.45), or major bleeding (RR 0.96, 95% CI 0.42 to 2.20, p = 0.93); it did increase the risk of atrial fibrillation (RR 4.69, 95% CI 2.17 to 10.12, p <0.0001). **(Am J Cardiol 2018;121:649–655)**

Cryptogenic stroke is estimated to account for approximately 25% of all ischemic strokes, and it is hypothesized that some of these strokes are venous thromboembolisms that cross to the arterial system through a patent foramen ovale (PFO).[1,2] After their first cryptogenic stroke, patients remain at increased risk of recurrent stroke and thus secondary prevention is crucial. Percutaneous device closure of a PFO can theoretically decrease the risk of recurrent stroke; however, despite multiple trials, it remains unclear if PFO closure provides any additional protection to medical therapy (MT) with antiplatelet and/or anticoagulation medication. Several randomized controlled trials (RCTs) have compared the efficacy of PFO closure and MT with MT alone to prevent recurrent stroke; however, their results are conflicting.[3–5] Similarly, previous meta-analyses of these trials have come to conflicting conclusions.[6–9] Presently, it is a class III recommendation to close a PFO in a patient with previous cryptogenic stroke unless there is evidence of deep vein thrombosis, in which case it is a class IIb recommendation.[10] Despite the lack of consensus from RCT data, a large body of observational studies and meta-analyses appears to conclude that PFO closure is superior to routine MT at preventing recurrent stroke.[11–13] So there remains much debate as to the optimal strategy to manage these patients. Recently, the results of 2 RCTs, and the long-term data of the previously reported Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT) study, have been published.[14–16] Our aim was to perform an updated meta-analysis and trial sequential analysis (TSA) to determine if PFO closure plus MT is superior to MT alone to prevent recurrent stroke.

Methods

This meta-analysis was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[17] A comprehensive literature search was performed by 2 independent reviewers (T.A. and H.T.) using the PUBMED and EMBASE databases. Search terms used were "patent foramen ovale" combined with "percutaneous device OR closure OR close" and "randomized OR randomization." Only original articles published in scientific, peer-reviewed journals were considered for inclusion. Titles and abstracts were first screened, then entire articles were assessed based on inclusion and exclusion criteria. The inclusion criteria were (1) study design: RCT; (2) patient population: previous cryptogenic stroke;

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See page 655 for disclosure information.

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CASE REPORT

CT-Guided Intranodal Lymphangiography for Postoperative Chylous Ascites

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Abstract The utility and minimal invasiveness of ultrasound-guided intranodal lymphangiography have already been reported by several researchers. Although ultrasound-guided intranodal lymphangiography is known to be not technically difficult in general, a patient's edematous groin due to hypoalbuminemia resulting from chylous ascites made it too challenging to detect and prick the lymph nodes precisely. This report describes a 71-year-old female with refractory chylous ascites due to an operation for an extrahepatic bile duct cancer, who was successfully treated by computed tomography (CT)-guided intranodal lymphangiography. After switching from ultrasound- to CT-guided lymphangiography, the procedure was successfully performed, and the refractory chylous ascites was treated.

Keywords Intranodal lymphangiography · Chylous ascites · Pylorus-preserving pancreaticoduodenectomy · Chylothorax · Lipiodol

Introduction

Chylous ascites may occur after abdominal surgery as a result of damage to the intraabdominal lymphatic vessels. Lymphangiography is known to be both diagnostic and therapeutic for chylous leakage. Ultrasound (US)-guided intranodal or inguinal lymphangiography is easier and more practical than pedal lymphangiography [1]. Nevertheless, thick edematous skin and massive ascites may hamper the precise detection of inguinal lymph nodes. We herein report a case of a postoperative chylous ascites treated by computed tomography (CT)-guided intranodal

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Case Report

CASE REPORT

Supratentorial acute subdural haematoma during microvascular decompression surgery: report of three cases

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Abstract

Supratentoiral haemorrhage during posterior fossa surgery is very rare. Authors report three cases of acute subdural haematoma occurred during microvascular decompression (MVD). Bleeding was observed in the suboccipital surgical area during operation but the origin of the bleeding was not confirmed intraoperatively in all cases. Decompression procedure was completed and immediate postoperative computed tomography revealed supratentorial subdural haematoma. This complication was observed during MVD in healthy young patients with hemifacial spasm in our cases. Flexion of the head with reduction of cerebrospinal fluid may have induced rotational movement of the cerebrum resulting in rupture of bridging veins, but no definitive mechanism that fulfils the clinical characteristics was clearly determined.

INTRODUCTION

Microvascular decompression (MVD) is widely accepted as an effective method to treat hemifacial spasm (HFS), trigeminal neuralgia (TN) and glossopharyngeal neuralgia (GPN), but the morbidity and mortality must be minimised because these conditions are not life-threatening. Unfortunately, serious complications can still occur in some patients, of which haemorrhagic event is one of the most dangerous complications and may result in significant morbidity and mortality. Intraoperative bleeding at a remote site is extremely rare, although some haemorrhagic complications following MVD have been reported [1–5]. We report three cases of intraoperative haemorrhage in the surgical field with unclear origin during MVD for HFS, in which computed tomography (CT) after the surgery confirmed supratentorial acute subdural haematoma (ASDH).

CASE DESCRIPTION

The three reported cases occurred among 1259 MVD procedures performed from 2006 to 2015, 852 for HFS, 386 for TN, 17 for GPN and 4 for tic convulsif, in 392 male and 867 female patients aged 19–86 years (mean age at operation 55.2 years). All operations for HFS were performed with a method described previously [6].

The patients' clinical characteristics are summarised in Table 1. In Case 1, bloody cerebrospinal fluid (CSF) was observed in the subdural space after opening the dura mater

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CASE REPORT

Diffusion-weighted imaging characteristics of methotrexate-induced acute encephalopathy

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Key Clinical Message

Methotrexate (MTX)-induced encephalopathy is a grave complication in patients with malignancies. The early diagnosis of acute encephalopathy was difficult by conventional computed tomography (CT), and T1- or T2-weighted magnet resonance (MR) imaging. We report that the diffusion-weighted (DW) imaging is useful for early detection of acute leukoencephalopathy.

Keywords

Diffusion-weighted imaging, encephalopathy, magnetic resonance imaging, methotrexate, neurotoxicity.

Introduction

The computed tomography (CT)/magnetic resonance (MR) image-based diagnosis of chronic irreversible leukoencephalopathy related to methotrexate (MTX) administration has been established. This disorder is known as a complication [1].

On the other hand, acute reversible leukoencephalopathy has not been widely recognized. Recent studies indicated the usefulness of diffusion-weighted MR images for the early diagnosis of acute leukoencephalopathy [2–4].

In this study, we report a patient who developed neuropathy through a rapid course after MTX administration and was diagnosed with acute leukoencephalopathy based on diffusion-weighted MR images, leading to a favorable course by the prompt discontinuation of MTX administration.

Case Report

A 53-year-old man was diagnosed as having lymphomatoid granulomatosis involving the central nervous system (CNS) and left lower lung. Because the CNS lesions worsened, the patient underwent treatments with rituximab (375 mg/m^2), MTX (3.5 g/m^2), procarbazine (100 mg/m^2/d/7 days), and vincristine (1.4 mg/m^2) (R-MPV therapy). Leucovorin rescue was given after high-dose MTX, with no delay of MTX excretion in any course. Intrathecal injections of MTX, cytarabine, and prednisolone were given three times as part of the R-MPV therapy. No complications, such as headache, neck stiffness, or vomiting, were observed. Eleven days after the third course of R-MPV therapy, sudden dysarthria occurred around noon, and rapidly deteriorating neurological symptoms, such as paralysis of the left extremities, decreased consciousness [*Glasgow Coma Scale (GCS); E (eye opening):2, V (best verbal response):2, M (best motor response):4*], and seizure, were apparent by night.

The next morning (day 12), MR imaging was performed (Fig. 1A). While there was no apparent spread of abnormal signals on T2-weighted or fluid-attenuated inversion recovery (FLAIR) images, high-intensity regions associated with symptoms of the left side of the body were noted in the right periventricular area and corona radiata on diffusion-weighted (DW) imaging, and MTX-induced acute leukoencephalopathy was

気道管理とその処置

Emergency airway management

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Akiko Ozawa

KEY WORDS
困難気道，緊急気道管理アルゴリズム，バッグ・バルブ・マスク換気，声門上気道デバイス，侵襲的気道確保

気道管理の考え方

生命維持に酸素は必須であり，安全で確実な気道管理は最優先となる。緊急時には瞬時に患者の酸素化と換気状態を把握し，酸素投与と応援要請を行って，アルゴリズムのどの段階にあり，どの器材を使用するのかを決定し，これらの情報をチームで共有すべきである[1]。

1. 酸素化の把握

経皮的酸素飽和度（SpO_2）は簡便に測定できるが，SpO_2が高値であるからといって換気状態が良好とはかぎらない[2][3]。SpO_2高値は「現在の体内の酸素量」を表しているに過ぎないうえ，体内の酸素量は患者背景により異なるため，「換気停止後，SpO_2は速やかに低下する」と考えて対応すべきである。低酸素状態は心停止につながり，SpO_2が低下してから準備をしたのでは遅い。

2. 換気状態の評価が重要

低酸素状態の回避に重要なのは，確実な気道確保と換気に他ならない。日本麻酔科学会では，換気状態の評価に重点を置いた気道管理のアルゴリズムを作成している（詳細は他稿を参照 p. 770）[4]。臨床現場での換気の評価としては，胸郭挙上や呼吸回路の曇りなどがあげられるが，このアルゴリズムではより客観的に評価するために，カプノグラムの波形で状態を判断する[4]。カプノグラムの波形が矩形波であれば換気は正常で「グリーンゾーン」，不十分な場合は換気困難で「イエローゾーン」，波形を確認できない場合は換気不能で「レッドゾーン」となる。

現在の換気状態から適切な器材を選択して手技を実施しつつ，「もし」うまくいかなかった場合の“二の手”，“三の手”についても考えながら手技を行うべきである。

気道管理のアルゴリズム

救急現場では，手術室とは異なり突然に緊急事態に直面することが多く，器材やモニター，マンパワーが足りないなど時間的・環境的に余裕がなく，不利である。そのため，事前に思考を整理して，器材の準備や使用方法の確認が必要となってくる。

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5

非挿管患者の鎮静教育
～マイケル・ジャクソンは，何故，死んでしまったのか～

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＜要　旨＞
米国麻酔科学会の「非麻酔科医のための鎮静・鎮痛薬投与に関する診療ガイドライン」で鎮静は全身麻酔の一部とされている．麻酔科研修で習得する，知識や技術（年齢，全身状態や合併症の把握，使用薬剤の知識・選択，呼吸状態の把握と気道管理方法，環境の整備，実施者（術者）との連携，急変時対応など）は鎮静教育そのもので，特に初期研修医には必須である．院外では，Procedural Sedation Course（処置の鎮静と鎮痛）や日本医学シミュレーション学会主催のセデーション実践セミナーなどが開催されている．鎮静教育体制の構築は喫緊の課題で，全身麻酔と全身管理に精通した麻酔科医が鎮静教育に関与することが求められている．

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キーワード：非挿管患者の鎮静教育，日本医学シミュレーション学会，処置の鎮静と鎮痛

1．鎮静時の事故は多い

米国麻酔科学会（American Society of Anesthesiologists：ASA）のClosed Claim解析では，鎮静に関する死亡例は手術室内よりも手術室外が多く，呼吸抑制が原因のことが多いとされている[1,2]．

本邦では，日本医療機能評価機構が医療事故情報収集等事業を行っている．同ホームページで「医療事故情報」「鎮静」をキーワードとして検索すると，2010年から2017年までに約800件の報告がある．人工呼吸管理中や夜間の譫妄に対する鎮静事例以上に，内視鏡室や血管造影室で自然気道下での処置，検査時の事故事例，気道管理に関する事故が多数報告されている[3]．

これらの報告から，近年，手術室外の鎮静事故が多く，大きな問題となっていることがわかってきた．各種の処置や治療を無麻酔または局所麻酔薬のみで行うことは，患者が苦痛を感じるだけでなく極度の緊張，不安が自律神経系に異常をきたし全身状態の悪化も起こり得る．診療上必要な鎮静を確実に安全に行う医療が求められている．

2．何故，鎮静時の事故が多いのか

鎮静を全身麻酔の一部と考えていないため多くの事故が発生している．

米国麻酔科学会の「非麻酔科医のための鎮静・鎮痛薬投与に関する診療ガイドライン」では鎮静

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Original Article

Venom and Antivenom of the Redback Spider (*Latrodectus hasseltii*) in Japan. Part II. Experimental Production of Equine Antivenom against the Redback Spider

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SUMMARY: This is the first report on large-scale experimental production of an equine antivenom against the redback spider (*Latrodectus hasseltii*) lived in Japan. We captured 10,000 redback spiders in Japan and prepared the toxoids of crude venom extract, mixed the toxoids with a mineral oil adjuvant, and immunized healthy horses repeatedly over a period of several weeks. Thereafter, we separated the horse plasma, purified the γ-globulin fraction, and stocked it as a purified antivenom concentrate. Consequently, we manufactured approximately 6,500 vials of a single-dose freeze-dried test lot from a portion of the purified γ-globulin fraction, equivalent to the extract derived from 520 spiders. This test lot had an antitoxin titer comparable to that of a similar drug commercially available overseas (a liquid preparation), and the other quality met all quality reference specifications based on the Minimum Requirements for Biological Products and other guidelines relevant to existing antivenom drug products in Japan.

INTRODUCTION

The redback spider (*Latrodectus hasseltii*), named in 1870, is one of the tropical/subtropical spider species found throughout Australia (1). Currently, this spider has identified in many other countries, with the first discovery in Japan recorded in Osaka in 1995. Since then, their habitat has expanded northwards annually, with their presence confirmed in the Kanto area, Tohoku, and as far north as Hokkaido. Human cases of bites of this spider have been reported in Japan since 1997; therefore, this spider is gaining increasing attention (2–5). The main symptom of the spider bite is severe pain at the bite location. The primary cause of pain has been thought to be the venom known as α-latrotoxin (LT), which is a protein with a molecular weight of 130,000 daltons, found in the spider's salivary glands (6).

In Australia, where this spider species was first identified, there were risks of developing severe or life-threatening conditions following the spider bite, if not treated with equine antivenom. Therefore, an antivenom, produced from horses immunized with redback spider venom was approved for commercial manufacturing and marketing in 1956, according to personal communication from bioCSL (Seqirus; Victoria, Australia); thus, it has been clinically used for over a half-century. A comparative study on the characteristics of LT from Australian redback spiders and that of Japanese spiders demonstrated that the 2 venoms did not differ physicochemically and immunologically (7). Currently in Japan, the overseas commercial antivenom drug product (liquid type; bioCSL) has been personally imported by a doctor as the representative investigator within the framework of the clinical research to treat people with spider bites.

However, in 2014, the antivenom drug product became temporarily unavailable through import, because alternative suppliers could not be identified (8). Therefore, we, as a scientific research group of the Ministry of Health, Labour and Welfare, formulated a plan to quickly produce an equivalent domestic product and secure a supply for the safety and peace of mind of the people (9,10). In summer 2014, we collected approximately 10,000 redback spiders from the Kansai area and manufactured an equine antivenom for the first time in Japan.

MATERIALS AND METHODS

Capture of redback spiders and purification of crude LT: From June through December 2014, a total of 11,403 redback spiders, including 10,186 from 480 sites in the Osaka Prefecture and 1,217 from several sites in Nishinomiya City, were collected in collaboration with the Pest Control Organization Osaka and the Environmental Health Division of Nishinomiya City. The captured spiders were killed by keeping them in a −20°C freezer, and the frozen spiders were sent to the Department of Medical Entomology at the National Institute of Infectious Diseases (NIID). The venom glands were individually excised from 10,007 female spiders. Zirconia beads (4 mm in diameter) were added and homogenized for approximately 30 s. After centrifugation at 10,000 rpm (KUBOTA 3740; KUBOTA, Tokyo, Japan) for 3

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Original Article

Venom and Antivenom of the Redback Spider (*Latrodectus hasseltii*) in Japan. Part I. Venom Extraction, Preparation, and Laboratory Testing

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SUMMARY: The redback spider (*Latrodectus hasseltii* Thorell) reportedly invaded Japan in September 1995. To date, 84 redback spider bite cases have been reported; 7 of these cases employed the antivenom. Antivenom has been imported from Australia in the past, but because of restrictions on exportation it was evident that nearly all of the antivenom present in Japan would expire during 2014. In 2014, a plan was proposed to experimentally manufacture and stockpile a horse antiserum for ourselves, using redback spiders indigenous to Japan. A total of 11,403 female spiders were captured alive: 1,217 from the vicinity of Nishinomiya City, Hyogo prefecture, and 10,186 from Osaka prefecture. Of these, 10,007 females were dissected, and the venom was extracted from the venom glands of individuals and subjected to crude purification to yield 4 lots, of which the majority was α-latrotoxin. Among them, a large amount of single lots with an estimated protein content of 236 mg is subsequently scheduled to be used for immunizing horses. We also determined lethal toxicity of the venom (LD_{50}: 9.17 μg per mouse), and established the assay for the determination of an anti-lethal titer of antivenom in mice.

INTRODUCTION

In September 1995 the redback spider (*Latrodectus hasseltii* Thorell) was first discovered in Takaishi City, Osaka prefecture (1, 2), in Yokkaichi City, Mie prefecture the following November, and in Miyakojima City, Okinawa prefecture that December (3). The distribution of redback spiders in Japan has since expanded. It has been shown to be established in a total of 43 prefectures in Japan until 2016 (4). The possibility that the distribution of this spider will continue expanding and that the population will continue increasing are causes for concern.

Since 1996, 84 redback spider bite cases have been reported (14 of these cases were reported in 2009), and 7 of these cases employed antivenom (5 and T. Hifumi, unpublished data). Native to Australia, the redback spider is known as a venomous species; there are 3,000 to 5,000 bite cases every year (6), and an antivenom is also used for the treatment. The antivenom produced in Australia has been imported for use in Japan. However, in recent years, importation from Australia has been limited. As a result, it became clear that nearly all of the antivenom present in Japan would expire during 2014.

A plan for experimental production and stockpiling of a horse antiserum in Japan was implemented using redback spiders indigenous to Japan. We captured redback spiders, extracted their venom glands, and crudely purified the venom. We then performed characterization analysis, determined the lethal toxicity of the venom (LD_{50}), and established the assay for the determination of anti-lethal titer of antivenom in mice.

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MATERIALS AND METHODS

Capture of redback spiders: A total of 11,403 female redback spiders were captured alive: 1,217 in the vicinity of Nishinomiya City, Hyogo prefecture, and 10,186 in Osaka prefecture (Fig. 1A and 1B). From June through December 2014, female spiders were captured alive in several sites close to Nishinomiya City and in 480 sites in Osaka prefecture. Every effort was made to capture individuals alive by hand using tweezers or with gloves. Pesticides were not used during capture, and specimens were killed by freezing at –20°C. The redback spiders stored in the freezer were transported frozen in various batches to the National Institute of Infectious Diseases (NIID), Tokyo, Japan. Dry ice was used during transport to prevent specimens from thawing.

Removal of the redback spider venom glands and crude purification of the venom: Because the venom gland is covered with a thick layer of muscle, the fangs

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Original Article

Freeze-dried equine-derived redback spider antivenom: a local irritation study by intramuscular injection in rabbits and a repeated-dose toxicity study in rats

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Abstract: The redback spider (*Latrodectus hasseltii*) is nonindigenous to Japan but has now spread throughout the country. Bites to humans are rare but can be fatal. We prepared freeze-dried redback spider antivenom for therapeutic use against bites in Japan by immunization of horse plasma. This study included two nonclinical tests of the antivenom: a local irritation study involving a single intramuscular administration to rabbits (with injections of physiological saline and an existing freeze-dried diphtheria antitoxin as control and comparison substances, respectively) and a 2-week repeated intermittent intravenous-dose toxicity study in rats. The irritation study showed the antivenom's irritancy to be comparable with that of the saline and the existing antitoxin preparations under the test conditions. In a repeated-dose toxicity study, no toxicity change was found in male or female rats, and the no-observed-adverse-effect level (NOAEL) was judged to be a dose volume of 20 mL/kg (1082 units/kg antivenom activity) in both male and female rats. In addition, there was no toxicological difference between proteinaceous diphtheria antitoxin and redback spider antivenom prepared to have the same protein content and the same additive composition. Based on these findings, we will further advance our research towards clinical application of the redback spider antivenom. This research was supported by the Research Program on Emerging and Re-emerging Infectious Disease of the Japan Agency for Medical Research and Development. (DOI: 10.1293/tox.2017-0053; J Toxicol Pathol 2018; 31: 105–112)

Key words: freeze-dried redback spider antivenom, equine polyclonal antibody, local irritation study, repeated-dose toxicity study

Introduction

Redback spiders (RBSs) (*Latrodectus hasseltii*) produce the venomous neurotoxin alpha-latrotoxin[1]. The RBS originated in Australia but has now been confirmed in New Zealand, various European countries, Southeast Asia, and the United States[2]. In Japan, it was first reported in 1995 in Takaishi City in Osaka Prefecture, Yokkaichi City in Mie Prefecture, and Miyakojima City in Okinawa Prefecture[3]. RBSs were first sighted in Metropolitan Tokyo in 2014, and they are rapidly becoming a nationwide problem in Japan[3]. We believe that there is a risk they will spread throughout East Asia due to climate change and intensive interaction between people.

Most physicians in Japan are unfamiliar with RBS bites, as they are rare occurrences, so there is only limited clinical experience[2]. The symptoms of the bites are usually mild and localized, such as localized pain and erythema[2]. However, before the development of a specific RBS antivenom (RBSAV), which is manufactured through the immunization of horses, these bites often proved to be fatal[4]. RBSAV is produced by the Commonwealth Serum Laboratories (CSL) in Australia, but at present, it is considered an

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③病棟でのインシデント対策

当院の不眠時におけるプロトコルに基づく薬物治療管理（PBPM）の実践

国立病院機構静岡医療センター　薬剤部[1)]、消化器科[2)]
稲葉　真実[1)]、彦坂　麻美[1)]、薄　雅人[1)]
滝　久司[1)]、小林　智晴[1)]、大西　佳文[2)]

病院紹介

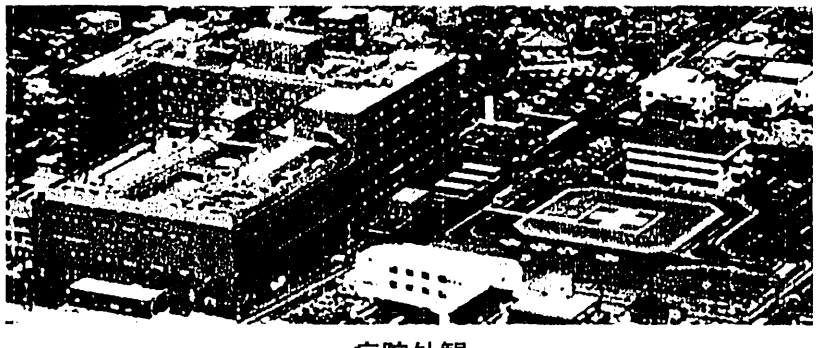
国立病院機構静岡医療センター（以下、当院）は、「循環器」、「がん医療」、「救急」および「総合診療」を4本柱として地域医療のニーズに応えています。平成29年10月には静岡富士病院の機能を当院に移転し統合し、これまでの急性期に加え神経難病・重症心身障害の方を中心にした慢性期医療にも貢献しています。

病院概要

標榜診療科：26診療科、病床数：450床
薬剤師：19名（治験管理室専任CRC 1名含む）（平成29年11月現在）
平成28年度薬剤部実績
院外処方せん発行率：96.1%
一般名処方加算１：27,367件、一般名処方加算２：17,833件
病棟薬剤業務実施加算１：16,769件、病棟薬剤業務実施加算２：500件
薬剤管理指導料１：5,458件、薬剤管理指導料２：5,979件

1．はじめに

入院患者は身体活動量の変化や不安などの精神状態、環境変化等により不眠を訴えることがある[1)]。特に、高齢者では睡眠薬を内服するケースが多くなっており[2)]、その際に選択される代表的な睡眠薬の一つであるベンゾジアゼピン系睡眠導入剤は筋弛緩作用を有するため転倒転落のリスク要因となる。入院患者の転倒転落は患者のQOL、ADLを低下させるとともに入院期間の延長など医療経済的にも問題視されている[3)]。また、ベンゾジアゼピン系睡眠導入剤による前向性健忘症、反跳性不眠、せん妄等の副作用発現のリスクも増加すると言われている[4)]。近年、多種多様な睡眠薬が上市されているが、適正な睡眠薬の選択のためには患者の不眠の分類（入眠障害、早朝覚醒、中途覚醒、熟眠障害等）や病態、年齢等を考慮することが重要となる。そこで、当院では不眠を訴



病院外観

原　著

急性心筋梗塞患者における心臓リハビリテーションが冠危険因子の目標達成に与える効果

Effects of cardiac rehabilitation on achievement of coronary risk factors goal in patients with acute myocardial infarction

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要　旨

【目　的】急性心筋梗塞（AMI）患者に対する回復期心臓リハビリテーション（心リハ）が，退院後4ヶ月時における各冠危険因子の目標達成に与える効果を検討した．

【方　法】対象をAMI患者215名（平均年齢65±11歳，男性178例）とし，4ヶ月間の回復期心リハを実施した心リハ実施群123例と，実施しなかった心リハ非実施群92例に分類した．対象の退院後4ヶ月時の各冠危険因子を調査し，二次予防のガイドラインの目標を達成しているか否かを評価した．各冠危険因子の目標を達成した割合を2群間で比較検討した．

【結　果】退院後4ヶ月時において，心リハ実施群のbody mass indexと禁煙の目標を達成した患者の割合は，心リハ非実施群と比較して有意に高値を示した（それぞれ$P<0.05$）．

【結　論】回復期心リハは，退院後の体重管理と禁煙の目標達成において有効であることが示唆された．

〔心臓リハビリテーション（JJCR）22（4）：269-273，2016〕

Key words：急性心筋梗塞，冠危険因子，心臓リハビリテーション

はじめに

急性心筋梗塞（AMI）患者において，冠危険因子の是正を通した二次予防の実施は，退院後の回復期における主目標とされている[1,2]．先行研究によると，回復期における運動療法と患者指導を含めた包括的心臓リハビリテーション（心リハ）は血圧，中性脂肪（TG），血糖値などの冠危険因子を改善することが報告されている[3~5]．

その一方で，AMI患者は，二次予防に関するガイドライン[6,7]における各冠危険因子の目標値を達成している割合が低いとされている[8,9]．先行報告によると，二次予防に関するガイドラインにおける低比重リポタンパクコレステロール（LDL-C）の目標値を達成しているAMI患者の割合は，退院後3ヶ月時で7割程度と報告されている[9]．AMI患者の二次予防においては，各冠危険因子の数値を改善し，ガイドラインの目標値を達成することが重要である[6]．よって，回復期心リハにおいてガイドラインの目標値の達成に向けた患者指導が必要であると考えられる．

しかし，回復期心リハの継続がガイドラインにおける冠危険因子の目標達成に及ぼす効果についての報告は少ない．そこで本研究は，回復期心リハの参加がAMI患者の退院後4ヶ月時における各冠危険因子の目標達成に与える効果を検討することを目的とした．

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Effects of exercise training on exercise capacity, cardiac function, BMI, and quality of life in patients with atrial fibrillation: a meta-analysis of randomized-controlled trials

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Exercise training has become part of the standard care for patients with cardiovascular disease. We investigated the effects of exercise training on exercise capacity, cardiac function, BMI, and quality of life in patients with atrial fibrillation (AF). We searched for randomized-controlled trials of supervised exercise training versus care without exercise training (the control) in patients with permanent or nonpermanent AF published up to November 2016. Standard mean differences (SMD) or mean differences (MD), and 95% confidence intervals (CIs) were calculated using random-effect models. We identified 259 trials, and after an assessment of relevance, five trials with a combined total of 379 participants were analyzed. In AF patients, exercise training significantly improved exercise capacity and left ventricular ejection fraction compared with the control (SMD: 0.91, 95% CI: 0.70 to 1.12; MD: 4.8%, 95% CIs: 1.56 to 8.03, respectively). Compared with the control, exercise training also significantly reduced BMI (MD: −0.47 kg/m^2, 95% CIs: −0.89 to −0.06) and significantly improved scores in the 'general health' and 'vitality' sections of the 36-item Short Form Health Status Survey (SMD: 0.71, 95% CIs: 0.30 to 1.12; SMD: 0.81, 95% CIs: 0.40 to 1.23, respectively). Exercise training improved exercise capacity, left ventricular ejection fraction, and some the 36-item Short Form Health Status Survey scores, and reduced BMI in AF patients. *International Journal of Rehabilitation Research* 40:193–201

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Keywords: atrial fibrillation, BMI, cardiac function, exercise capacity, exercise training, meta-analysis, quality of life

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in adults. According to observational studies, the prevalence and incidence of AF have increased markedly over the past 50 years (Schnabel *et al.*, 2015). AF is associated with increased mortality, mainly because of the increased risk of stroke and heart failure (HF) (Schnabel *et al.*, 2015). Rhythm control therapies such as antiarrhythmic drug therapy (ADT), electrical cardioversion, or pulmonary vein isolation are used in AF patients to restore and maintain sinus rhythm (Kirchhof *et al.*, 2016). However, ADT and electrical cardioversion are frequently ineffective and may be associated with serious adverse effects (Pappone *et al.*, 2006). Although pulmonary vein isolation is more effective for the restoration and maintenance of sinus rhythm than ADT in selected AF patients, the relatively high recurrence rate remains a significant limitation (Pappone *et al.*, 2006). Therefore, some AF patients continue to have disordered sinus rhythm even after rhythm control therapies.

Previous studies have reported that AF patients have an increased risk of a decline in physical performance including exercise tolerance (Magnani *et al.*, 2016). Exercise intolerance is one of the major symptoms among AF patients and is a poor prognostic indicator among HF patients with AF (Atwood *et al.*, 2007). Moreover, exercise intolerance leads to weight gain, resulting in the deterioration of overall health status (Blair and Brodney, 1999). In addition, AF reportedly reduces left ventricular (LV) function and decreases quality of life (QOL) (European Heart Rhythm Association1; European Association for Cardio-Thoracic Surgery, 2010). Therefore, comprehensive management, including exercise training, is extremely important for AF patients.

Recently, exercise training has become part of the standard care for patients with heart disease. The benefits of long-term exercise training are well described in patients with HF, myocardial infarction, or coronary artery bypass grafts (Hegbom *et al.*, 2007). However, exercise training in AF patients has received little attention in the literature. Given the limited evidence, physicians and other health care providers may hesitate to recommend exercise training to AF patients. Therefore, it is necessary to determine the effects of exercise training among AF

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高齢慢性心不全患者に対する心臓リハビリテーション

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鬼頭和也[3)]，濱貴之[3)]，角谷星那[3)]，田邊潤[2)]

要旨

近年，生活習慣の欧米化に伴う虚血性心疾患の増加に加え，高齢化による高血圧や心臓弁膜症の増加などの疾病構造の変化により，心不全患者が心臓リハビリテーション（心リハ）の主たる対象を占めるようになってきた．多くの心不全患者は70歳以上の高齢者で，原疾患として虚血性心疾患が多く，そして高血圧，糖尿病，慢性腎臓病のみならず運動器疾患や認知症など多数の併存疾患を合併している．また，高齢慢性心不全患者はフレイルの構成要素との関連が強く，容易にフレイルになり得るとされている．高齢慢性心不全患者の心リハでは，個々の症例において心不全の病態把握と併存疾患を含む患者の特徴を的確に捉え，リスクの層別化を念頭に置き対応することが必要である．また，高齢慢性心不全患者の心リハ介入におけるアウトカムの設定は，運動耐容能や長期予後とは異なる指標の設定が必要である．アウトカムは，再入院はもちろん転倒，脆弱性骨折も含めて，そのサロゲートマーカーである筋力，筋量，歩行スピードあるいは日常生活動作を使用することが望まれる．

キーワード：心臓リハビリテーション，心不全，高齢者

1．心臓リハビリテーションの歴史

心臓リハビリテーション（心リハ）は，急性心筋梗塞（AMI）の安全な治療と管理を目的に，1950～60年代に米国で始まり発展した．それまでのAMIの治療の中心は，数週間に及ぶ安静であったが，臥床による身体機能のディコンディショニングが知られるようになり，徐々に早期離床が試みられるようになった[1)]．1980年代以降は薬物療法の発展や，再灌流療法の普及により，冠動脈疾患の急性期治療は大きく変化し，安全かつ早期に離床が可能となった[1)]．さらに90年代後半には，ステントを使用した冠動脈血行再建術が一般化しAMI患者の早期離床が容易となったことで，ディコンディショニングの弊害は大幅に減少した[1)]．その結果，急性期の心リハの期間は短縮され，AMIの心リハは急性期のディコンディショニング予防から，回復期の二次予防へその役割を変え，現在ではQuality of life（QOL）と予後の改善に重点が置かれている．このように，心リハはAMI患者の治療と共に発展してきた．

2．慢性心不全患者の増加と心リハ対象者の変化

一方で近年，心リハの対象となる疾病や患者の特徴が大きく変化している．生活習慣の欧米化に伴う虚血性心疾患の増加に加え，高齢化による高血圧や心臓弁膜症の増加などの疾病構造の変化により，慢性心不全（CHF）患者が増加し，心リハの主たる対象を占めるようになってきている．心血管疾患の終末像であるCHFは，長寿が達成された先進国の代表的な疾患であり，特に老年期に急増する[2)]．本邦の疫学調査によると，CHFの患者数は2005年の97万9千人から，5年ごとに9万人ずつ増加して，2030年には130万人を超過すると予測されている[3)]．

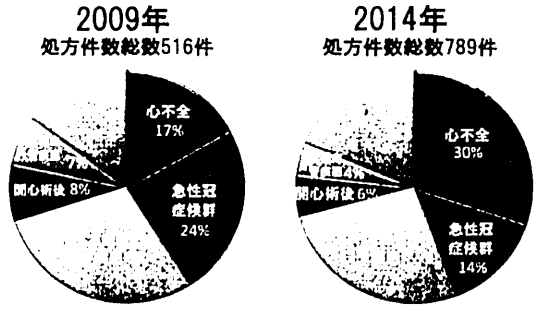

図1　静岡医療センターにおける2009年度と2014年度の心臓リハビリテーション対象疾患の比較

1）常葉大学 静岡
2）国立病院機構 静岡医療センター 臨床研究部
3）国立病院機構 静岡医療センター リハビリテーション科

学会印象記

●Asia Western Pacific Region of World Confederation for Physical Therapy (WCPT-AWP) Congress 2017

アジア・西太平洋地域において日本の理学療法士は何ができるのか？

常葉大学健康科学部静岡理学療法学科
加藤倫卓

はじめに

2017年6月27～30日の日程で開催された，Asia Western Pacific Region of World Confederation for Physical Therapy(WCPT-AWP) Congress 2017に参加した．本学会は4年に一度行われ，アジアおよび西太平洋周辺諸国で最大の理学療法学会である．この地域の理学療法士の協力体制を高めることを目的にしており，今回はタイの首都バンコクで開催された．

本学会では，長寿と健康の持続を推進するために，各国の理学療法士の知恵，知識，そして優れた実践スキルを統合しようと，“Moving towards health, longevity, and sustainability(健康，長寿，そして持続可能性への推進)”というテーマが掲げられていた．今回，本学会においてoral presentationを行った経験と，本学会を通して考えさせられたことなどを書き記したいと思う．

抄録がアクセプトされるまでの珍しい経験

通常，学会発表するには，抄録を提出して査読を経た後にアクセプトされるのだが，今回この過程で少し珍しい経験をした．抄録を提出してから約2か月後に学会側から査読結果が来たが，“Accepted after revisions request in comments (査読コメントに対して修正後にアクセプト)”と記されていた．これまでの経験上，抄録の修正要求は初めてであったが，査読者のコメントに応じて丁寧に修正し，早速再投稿をした．すると翌日には“Accepted for oral presentation”のメールが届いた．“再提出した抄録の確認をしているのかな？”と少々疑問を抱きつつも，アクセプトされたことには安心した．

図1　筆者のoral presentationの様子

この件について学会期間中に他の研究者に尋ねてみたところ，修正要求の連絡自体がない者から，2度も修正を要求された者までいたことがわかった．ちなみに，本件に関しては投稿規定に何も記載されておらず，われわれのなかでは開催国のローカルルールということで話は片付いたが，真相は不明である．

開会式セレモニー

学会の開会式は，タイの王女であるPrincess Sirindhornの挨拶と講演から，厳かな雰囲気で始まった．王女は，タイにおける理学療法の教育環境，健康増進のために必要なこと，そしてテクノロジーを利用したヘルスケアシステムに関することをお話しされた．約20分にも及んだ王女の熱弁は，国際学会の開会式にふさわしいセレモニーとなった．

印象に残った講演

本学会は通常の学会と同様，教育講演，シンポジウム，口述およびポスター演題発表，そしてワークショップから構成されていた．いくつかの講演を聴いたが，そのなかで印象に残った講演を2つ挙げたいと思う．

1つ目は，大学カリキュラムや理学療法学生の学びについて研究をしているオーストラリアのメルボルン大学のGillian Webb先生による，“健康，長寿，そして持続可能性の推進における理学療法教育のあり方”についての講演である．一般市民がよりよい健康状態を達成するためには多職種によるチームアプローチが重要で，理学療法士はそのチームのリーダー的存在になるべきであり，また，チームのリーダーを育成するためには，大学におけるカリキュラムの構成内容が重要であるこ

図2　学会場にて
左から2番目が筆者．

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Original Article

Relationship between advanced glycation end-product accumulation in the skin and pulmonary function

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Abstract. [Purpose] This study aimed to evaluate the relationship between advanced glycation end-product accumulation and pulmonary function in a general population with normal spirometry results. [Subjects and Methods] A total of 201 subjects (mean age, 56 ± 11 years; males, 58%) enrolled in this study. Subjects were classified into two groups (younger group [<65 years old] and elderly group [≥65 years old]). Skin autofluorescence was assessed as an estimate of advanced glycation end-product. Forced vital capacity and forced expiratory volume in one second were measured using a spirometer, and the forced expiratory volume in one second/forced vital capacity ratio (FEV1/FVC) was calculated. [Results] Skin autofluorescence was not an independent factor associated with FEV1/FVC in the younger group, but both skin autofluorescence and pack-years of smoking were significant independent factors associated with FEV1/FVC in the elderly group. [Conclusion] Advanced glycation end-product accumulation, assessed by skin autofluorescence, is an independent factor negatively associated with FEV1/FVC in elderly people with normal spirometry results.

Key words: Advanced glycation end product, FEV1/FVC, Elderly

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains a major public health problem and is projected to rank fifth in global disease burden by 2020[1]. COPD is induced by long-term cigarette smoking, and is primarily characterized by the presence of airflow limitations resulting from airway inflammation and remodeling and the development of emphysema[2]. Chronic inflammation occurs not only in the airways of COPD patients, but throughout the body as well, given that inflammatory mediators are known to spread from the lung to the rest of the body[2].

According to recent studies, the level of advanced glycation end products (AGEs) increases with age and is higher in smokers and COPD patients[3, 4]. AGEs are bioactive molecules formed by the nonenzymatic glycation or peroxidation of proteins, lipids, and nucleic acids[5, 6]. AGEs increase inflammation by binding to receptors for AGE (RAGE), which are present on cell surfaces in tissues[5, 7]. Therefore, AGE accumulation may play a role in the pathogenesis of COPD by increasing inflammation[8].

Several AGEs, such as pentosidine and Nε-(Carboxymethyl)-L-lysine (CML), have been reported to emit a characteristic fluorescence in human skin[9]. AGEs assessed by skin autofluorescence (SAF) could help in the rapid evaluation of AGE

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終わりに

本指針は、2008年度（平成20年度）に作成された「災害時難病患者支援計画を策定するための指針」を改訂したものである。

厚生労働省は2005～2007年度（平成17～19年度）、「重症難病患者の地域医療体制の構築に関する研究」班（主任研究者：東北大学　糸山泰人教授）を組織し、重症神経難病患者を主な対象とした「災害時における難病患者対策」を検討するプロジェクトチームを結成した。2008年（平成20年）、プロジェクトリーダーであった新潟大学　西澤正豊教授により、「災害時難病患者支援計画を策定するための指針」が作成された。その目的は、行政機関が平常時、および、災害時における難病患者の支援計画を策定するための指針として用意されたものである。その後も、災害対策チームは引き継がれ、2016年度（平成28年度）からは「難病患者の地域支援体制に関する研究」班（研究代表者：新潟大学　西澤正豊名誉教授）で、検討を続けている。

わが国は、2008年（平成20年）以降、さまざまな災害に見舞われている。2011年（平成23年）東日本大震災という未曾有の大災害の後、熊本地震、鳥取地震、集中豪雨と河川の氾濫や大規模な土砂崩れなど、多くの災害に見舞われている。こうした中で、2013年（平成25年）には災害対策基本法、および災害救助法が改正され、2016年（平成28年）には防災基本計画が示された。中でも、災害対策基本法では、災害時要配慮者への支援として、市町村に災害時避難行動要支援者の名簿の作成が義務づけられ、個別計画の策定が求められていることは特筆すべきことである。

2013年（平成25年）には「障害者総合支援法」、2015年（平成27年）には「難病患者に対する医療等に関する法律」（難病法）が施行され、難病患者にもさまざまな変化が訪れている。しかし、依然として、難病行政が都道府県と市町村の狭間にあるため、災害対策の中で、都道府県と市町村の緊密な連携と情報共有が必要である状況は変わっていない。

本指針の目的は、保健所（健康福祉センター）を中心として都道府県と市町村が連携して、難病患者の災害対策、とくに、避難行動要支援者個別計画の策定を推進していくことである。幸い、「災害時難病患者支援計画を策定するための指針」（2008年（平成20年））により、都道府県が作成した地域防災計画や個別計画策定のための指針等の中で、難病患者が要配慮者として認識されるようになってきた。こうした流れを個別支援計画の策定に結びつけていくことが私たち難病医療に携わる医療者の願いである。

2017年（平成29年）８月

厚生労働科学研究費補助金　難治性疾患等克服研究事業
難治性疾患等政策研究事業（難治性疾患政策研究事業）
「難病患者の地域支援体制に関する研究」班
同「難病患者の災害対策のあり方」
グループ代表　溝口　功一

編集後記

平成 29 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、誠にありがとうございます。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、改めて感謝申し上げます。最後に事務の渡邉光子さん。毎年毎年、今年こそは時間に余裕をもって仕事を仕上げようと思うのですが、今年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。

2018 年 9 月

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