同　意　撤　回　書

東京大学医学系研究科長・医学部長　殿

研究課題「結合織疾患（遺伝性素因を含む）を背景とした大動脈瘤・解離に対する外科治療成績の前向き検討多施設共同研究」

私は、上記研究への参加にあたり、説明文書の記載事項について説明を受け同意しましたが、同意の是非について再度検討した結果、同意を撤回いたします。

資料（試料）等の保存について（これまでの同意の状況）:「はい」または「いいえ」にご自身で○を付けてください。

提供した資料（試料）等が、長期間保存され、将来、新たに計画・実施される研究に使用されることに同意しました。

はい（本研究終了後も保存）　　いいえ（本研究終了時に廃棄）

資料等の保存について（同意の撤回）:

「はい」または「いいえ」にご自身で○を付けてください。

提供した資料（試料）等が、長期間保存され、将来、新たに計画・実施される研究に使用されることへの同意を撤回いたします。

はい（本研究終了時に廃棄）　　いいえ（本研究終了後も保存）

平成　　年　　月　　日

氏名（研究参加者本人または代諾者）（自署）＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

（代諾者の場合は、本人との関係）＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

0	No,	2011 年 秋 ―

JCVSD データ利用申請書

下記、質問事項を全て　　記入欄にパソコンにてご記入ください。全て必須です。

■管理情報

1	提出日 （年月日）	2012 年　　12 月　　21 日	
2	利用区分 （A or B）	B	
3	申請者区分 ＊該当する箇所に○	参加施設	大学病院 ・ その他施設
		非参加医療系施設	病院 ・ 大学 ・ 大学以外の研究機関
		協賛企業	医療系企業 ・ その他企業
		非協賛企業	医療系企業 ・ その他企業
		個人	研究者 ・ 学生 ・ 弁護士
		団体	官公庁 ・ 地方自治体 ・ 患者会
		その他	

■JCVSD 参加情報 ＊参加施設のみ記入

4	参加施設名	慶應義塾大学病院、三井記念病院・東京大学医学部附属病院
5	施設 ID	H － 0086
6	JACVSD に参加した年度	2006/10/2
7	前年度と前々年度の登録状況 （完了・A～D）	前年度（2011 年） 完了、前々年度（2010 年） A

■プロジェクト担当者情報

8	プロジェクト名 （研究タイトル）	結合織疾患（遺伝性素因を含む）を背景とした大動脈瘤・解離に対する外科治療成績の前向き検討
9	主任研究者名 （責任者）	志水　秀行 1)
10	共同研究者名 （全員）	志水　秀行 1)、高本　眞一 2)、本村　昇 3)、志水　秀行 1)、平田　恭信 3)、竹谷　剛 2)、鈴木　亨 3)、澤城　大悟 3)
11	所属機関名	1)慶応義塾大学病院、2)三井記念病院、3)東京大学医学部附属病院
12	部署	1)心臓血管外科、2)心臓血管外科、3)心臓外科・循環器内科・ユビキタス予防医学講座
13	住所	〒160-8582 東京都新宿区信濃町 35 番地
14	連絡担当者	志水　秀行

15	連絡担当者 E-mail	shimizu.md@gmail.com
16	連絡担当者 TEL	03-3353-1211
17	研究資金 (科研費・校費・寄付金・その他)	厚生労働省科学研究費 H24-難治等(難)-一般-051、他

■データ解析情報

18	使用データベース (成人・先天性)	成人
19	リサーチ内容 (例:)	結合織疾患(遺伝素因)を有する大動脈瘤・解離症例・家系の集積とその継続的な経過追跡・解析を行う為のレジストリー構築を目的とし、対象疾患群の最も侵襲的治療としての外科治療成績・術前周術期状態を分析する。本疾患群の大動脈手術のリスク要因としての解析を前向き、多施設共同検討として開始・検討する。
20	その背景・根拠 (例:)	動脈瘤・大動脈解離は発症すれば極めて死亡率が高く、またその死亡者数は増加傾向にあるにもかかわらずあまり注目されていない。結合織異常のマルファン症候群は大動脈瘤・解離を合併する代表的な疾患であるが、同疾患については遺伝的背景の解析が進んでいるものの非マルファン症候群症例における大動脈瘤・解離についてはその遺伝子異常、発症病態等についてほとんど情報が得られていないのが現実である。これら大動脈解離・大動脈瘤の中には遺伝的要素の強い家族集積性を認める大動脈瘤・大動脈解離の症例・家系があり、発症メカニズムのモデルとしてその遺伝子異常の解析や遺伝・発症形態の解析は多くの情報をもたらすことが予想される。さらに同疾患群には外科治療が最終治療手段となることも多い。しかしながら日本におけるそれら症例・家系についての解析は少数の限られた症例報告が多く遺伝形態の本態や治療に対する反応、予後についての情報は得られ難い状況となっている。また大動脈疾患による死亡率は 8.5 人/10 万人程度であり各医療施設単体での年間集積症例数はそれ程多くはなく、本症候群の本態の把握には症例・家系の集積とその継続的な経過追跡・解析を行う為の共通基盤の整備が必須と考えられている。 現在既に、平成 23 年度より当データベースを利用し、後ろ向き研究として結合織疾患合併症例の大動脈手術に対してのリスク要因としての解析を行い、マルファン症候群・非マルファン症候群それぞれの特徴等有用な解析結果を得ている。今後、同研究を基に東京近在の主要大動脈手術施行病院を参加施設として前向きな症例登録・追跡の開始及び評価項目の拡充が必要と考えられる。
21	対象となる母集団・除外集団 (例:母集団:Aorta のデータ、死亡症例除外など)	大動脈(弁・基部)置換術・修復術を施行した遺伝的素因を有する大動脈瘤・解離症例であるマルファン症候群だけでなく、周辺疾患群として大動脈炎・川崎病・Behcet・その他の膠原病(エーラスダンロス症候群・ロイツディーツ症候群等も含める。
22	解析対象期間 (例:2005 年 1 月～12 月)	2013 年 3 月 1 日 ～ 2018 年 2 月 28 日

23	対象項目 (例:　　)	年齢・性別・家族歴・併存疾患・発症状況・症状経過・血行動態・診断・施行術式・急性期および慢性期の薬物療法、CT・MRI・エコー所見による大動脈径変化、および術後合併症の発症状況・予後(全死亡・大動脈関連死亡・再入院)、L/D: 血清クレアチニン、CRP、Hb。
24	解析方法 (解析結果予測)	事務局と話し合いの上決定
25	解析結果を受け取りたい締切り	2013 年 12 月末日
26	以上の情報で不十分な場合は別紙にリクエスト・データ解析の仕方などを要約して提出すること	

■利用について

27	目的 (学術利用・臨床利用・out put の方法)	長期的には論文発表を行い、さらには、結合織疾患(遺伝的素因)を背景とした大動脈瘤・大動脈解離の共通基盤を基にしたレジストリー構築を目標とし、将来的に日本における大動脈瘤・大動脈解離のレジストリーとして発展させる。本疾患の生命的危険に至る前での早期発見、効果的な外科的また薬物治療の選択・開発、効果的な経過観察の方法の抽出またサロゲートマーカー等の評価等に継げる事を最終的な目標としている。
28	投稿予定の論文 (ある場合)	未定
29	発表予定の会議・学会の日程 (ある場合)	2013 年 4 月　アジア心臓血管外科学会
30	データが最終的に営利利用される場合はどのように利用されるか(出来るだけ詳しく)	該当せず

■実績・バックグラウンド

31	貴施設で、今回解析対象となる症例は年間に何例あるか また、主任研究者は今回解析対象となる症例を何例くらい経験しているか	一年間に施行する胸部大動脈瘤手術数は、慶應義塾大学病院が〇-〇例、三井記念病院心臓血管外科が 30-50 例、東京大学心臓外科が 50-80 例程度であるが、結合織疾患を背景とした大動脈瘤・大動脈解離はそのうちの数～十数%にとどまる。主任研究者は、これまでに約〇〇例の胸部大動脈瘤の手術経験を持ち、その約〇割は結合織疾患を背景とした大動脈瘤・大動脈解離であった。
32	これまでに、今回と同様または関連性の高いリサーチを行ったことがある場合は詳細を記入 (例:学会発表、論文名など)	・Shimizu H, Hachiya T, Yamabe K, Yozu R. Hybrid arch repair including supra-aortic debranching on the descending aorta. Ann Thorac Surg 2011; 92(6): 2266-8・Miyairi T, Kotsuka Y , Morota T, Kubota H, Shibata K, Ikeda,Y, Kitamura T, Kashima T, Takamoto S : Paraplegia after open surgery using endovascular stent graft for aortic arch aneurysm. J Thorac Cardiovasc Surg 2001;122:1240-1243 ・Shimizu H, Yozu R. Current strategies for spinal cord protection during thoracic and thoracoabdominal aortic aneurysm repair. Gen Thorac Cardiovasc Surg 2011;

		59: 155-63 ・Miyairi T, Kotsuka Y , Ezure M, Ono M, Morota T, Kubota H, Shibata K, Ueno K, Takamoto S : Open Stent-Grafting for Aortic Arch Aneurysm is Associated with Increased Risk of Paraplegia. Ann Thorac Surg 2002; 74:83-9 ・Suzuki T, Trimarchi S, Sawaki D, Grassi V, Costa E, Rampoldi V, Nagai R, Eagle K. Circulating TGFbeta levels in acute aortic dissection. J Am Coll Cardiol, 2010, ・Suzuki T, Eagle Kvet al. Diagnosis of acute aortic dissection by D-dimer; the IRAD-Bio experience. Circulation. 2009;119:2702-2707,
33	今回解析対象となる領域においての実績、バックグラウンド、アピールポイントなどがあれば記入 (例:研究会に所属している、班研究を作ったなど)	・共同研究者(鈴木亨)は大動脈解離の国際レジストリーの構成員であり大動脈疾患の臨床情報統計に精通している。 ・平成 23 年度厚生科研費「家族性大動脈瘤・解離の実態解明・効果的な進行予防・治療を目的としたレジストリー構築に関する研究(H23-難治-一般-047)」の一環として「結合織疾患(遺伝性素因を含む)を背景とした大動脈瘤・解離に対する外科治療成績の検討」を開始している。 ・平成 24 年度厚生科研費「大動脈疾患症例の実態解明・効果的な進行予防・治療を目的とした全国的統一基盤システムの構築と研究(H24-難治等(難)-一般-051)」が採択され、研究班が構成されている。
34	備考	

【注意事項】

■利用申請の基準　※下記を満たす施設のみ応募可

1. 2009 年－2010 年の登録が完了した施設
2. 科長、データマネージャー　※それ以外（科長、医局員、研究員、その他）の場合、応相談

■データ利用の区分

データ利用 A：既に登録されているデータの利用のみでプロジェクトを行う
データ利用 B：追加のデータ入力を行ってデータ分析を行う　※詳細 HP

■応募数

データ利用 A：1 施設 2 テーマ程度
データ利用 B：複数のテーマの応募可

■応募締切り

データ利用 A：2011 年 9 月 10 日(土)
データ利用 B：随時募集

■現在採択済みのプロジェクト

ホームページ参照　https://endai.umin.ac.jp/islet/jacvsd/P06.html#03

■申請先

必要事項を記入の上、メールにて申請　事務局 E-mail:　jacvsd-adm@umin.ac.jp

【データ利用の手順】

JCVSDO に申請書をメール

データ利用検討委員会にて審議

利用許可　　利用に問題有り

調整　　調整困難

ミーティング　　利用不可

解析

受け渡し

公表物の作成

公表物のチェック

公開

資料4:JACVSD日本心臓血管外科学会倫理委員会承認書

2009年4月1日

日本心臓血管外科手術データベース機構
代表幹事　　高本　眞一　殿

研究倫理審査申請書の審査結果について

貴機構から申請(平成21年2月12日付)のありました「日本心臓血管外科手術データベース」の研究倫理について、審査し、問題なしとの結果となったことを通知いたします。

特定非営利活動法人日本心臓血管外科学会
医療倫理委員会　委員長　　島本　光臣

倫理委員会個別審査判定表

審査番号　No. 10408

ヒアリング日時：　平成26年02月24日 18:30 - 18:50

説明者：　澤城 大悟

審査委員名：　主査：　竹下 克志　　副査：　山末 英典　　記入者：　竹下 克志

審査日：

＜1回目 判定＞　平成26年02月24日　：　承認

1）本研究の目的、プロトコールは科学的に妥当であるか

■はい

□いいえ→　　□適切に改訂された

2）被験者への侵襲は許容範囲か

■該当なし　□はい

□いいえ→　　□適切に改訂された

3）研究により起こりうる事故に対して適切な処置ができる体制にあるか

■該当なし　□はい

□いいえ→　　□適切に改訂された

4）薬物等を使用する場合、安全性は確立されているか

■該当なし　□はい

□いいえ→　　□適切に改訂された

5）対象の例数、研究期間の記載はあるか

■はい

□いいえ→　　□適切に改訂された

6）被験者への説明書、同意書の内容は整っているか

□該当なし　■はい

□いいえ→　　□適切に改訂された

7）被験者のプライバシーは守られているか

■はい

□いいえ→　　□適切に改訂された

8）「利益相反」については問題ないか

□該当なし　■はい

□いいえ→　　□適切に改訂された

9）試料、データの保管方法、期間は妥当であるか

■はい

□いいえ→　　□適切に改訂された

10）未成年者、判断能力のない成年が対象の場合、同意書の取り方は妥当であるか

□該当なし　■はい

□いいえ→　　□適切に改訂された

11）研究費の出所、使用法は妥当であるか

■はい

□いいえ→　　□適切に改訂された

12）議事要録の公表に伴い申請者の氏名等も公表されるが、研究課題の開示に異存はないか

■ない

□あり→　　□適切に改訂された

13）本委員会に提出すべき添付資料の確認
「倫理委員会に提出された資料のうち、本委員会での審議には不要の資料：
（有る場合）：該当試料番号　　」

＜問題点と改善のための指示事項＞

□適切に改訂された

＜コメント＞

□適切に改訂された

平成26年02月25日

倫理委員会個別審査判定表

審査番号　No.10408

ヒアリング日時：　平成26年02月24日 18:30 - 18:50

説明者：　澤城 大悟

審査委員名：　主査：　竹下 克志　　副査：　山末 英典　　記入者：　山末 英典

審査日：

＜1回目 判定＞　平成26年02月24日　：　承認

1）本研究の目的、プロトコールは科学的に妥当であるか

■はい

□いいえ→　　□適切に改訂された

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□該当なし　■はい

□いいえ→　　□適切に改訂された

3）研究により起こりうる事故に対して適切な処置ができる体制にあるか

□該当なし　■はい

□いいえ→　　□適切に改訂された

4）薬物等を使用する場合、安全性は確立されているか

■該当なし　□はい

□いいえ→　　□適切に改訂された

5）対象の例数、研究期間の記載はあるか

■はい

□いいえ→　　□適切に改訂された

6）被験者への説明書、同意書の内容は整っているか

□該当なし　■はい

□いいえ→　　□適切に改訂された

7）被験者のプライバシーは守られているか

■はい

□いいえ→　　□適切に改訂された

８）「利益相反」については問題ないか

■該当なし　□はい

□いいえ→　　□適切に改訂された

９）試料、データの保管方法、期間は妥当であるか

■はい

□いいえ→　　□適切に改訂された

10）未成年者、判断能力のない成年が対象の場合、同意書の取り方は妥当であるか

□該当なし　■はい

□いいえ→　　□適切に改訂された

11）研究費の出所、使用法は妥当であるか

■はい

□いいえ→　　□適切に改訂された

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■ない

□あり→　　□適切に改訂された

13）本委員会に提出すべき添付資料の確認
「倫理委員会に提出された資料のうち、本委員会での審議には不要の資料：
（有る場合）：該当試料番号　　」

＜問題点と改善のための指示事項＞

■適切に改訂された

＜コメント＞

□適切に改訂された

平成26年02月25日

倫　理　委　員　会
審 査 結 果 報 告 書

平成26年03月14日

申請者（研究責任者）
ユビキタス予防疫学寄付講座
特任助教
澤城 大悟　殿

東京大学大学院医学系研究科長・医学部長
宮園　浩平

審査番号　10408

研究課題　結合織疾患（遺伝性素因を含む）を背景とした大動脈瘤・解離に対する外科治療成績の前向き検討多施設共同研究

上記研究計画を平成26年03月10日の委員会で審査し下記のとおり判定しました。
ここに通知します。

判　定

○承認する　　条件付きで承認する
変更を勧告する　　承認しない
該当しない

研究成果の刊行に関する一覧表

雑誌

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Bossone E, Corteville DC, Harris KM, Suzuki T, Fattori R, Hutchison S, Ehrlich MP, Pyeritz RE, Steg PG, Greason K, Evangelista A, Kline-Rogers E, Montgomery DG, Isselbacher EM, Nienaber CA, Eagle KA.	Stroke and outcomes in patients with acute type A aortic dissection.	*Circulation.* 2013, 128: S175-9.
Larsen M, Bartnes K, Tsai TT, Eagle KA, Evangelista A, Nienaber CA, Suzuki T, Fattori R, Froehlich JB, Hutchison S. Sundt TM. Ja	Extent of preoperative false lumen thrombosis does not influence long-term survival in patients with acute type a aortic dissection.	*J Am Heart Assoc.* 2013, 2：e000112.
Miyairi T, Miyata H, Taketani T, Sawaki D, Suzuki T, Hirata Y, Shimizu H, Motomura N, Takamoto S.	Risk model of cardiovascular surgery in 845 marfan patients using the Japan adult cardiovascular surgery database	*Int Heart J.* 2013, 54: 401-4.
Yoshitake A, Shimizu H, Kawaguchi S, Itoh T, Kawajiri H, Yozu R	Hybrid repair of subclavian-axillary artery aneurysms and aortic arch aneurysm in a patient with Marfan syndrome.	Ann Thorac Surg. 2013, 95(4): 1441-3,

Pulse Pressure and Type A Acute Aortic Dissection In-Hospital Outcomes (from the International Registry of Acute Aortic Dissection)

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Little is known about the relation between type A acute aortic dissection (TAAAD) and pulse pressure (PP), defined as the difference between systolic and diastolic blood pressure. In this study, we explored the association between PP and presentation, complications, and outcomes of patients with TAAAD. PP at hospital presentation was used to divide 1,960 patients with noniatrogenic TAAAD into quartiles: narrowed (≤39 mm Hg, n = 430), normal (40 to 56 mm Hg, n = 554), mildly elevated (57 to 75 mm Hg, n = 490), and markedly elevated (≥76 mm Hg, n = 486). Variables relating to index presentation and in-hospital outcomes were analyzed. Patients with TAAAD in the narrowed PP quartiles were frequently older and Caucasian, whereas patients with markedly elevated PPs tended to be male and have a history of hypertension. Patients who demonstrated abdominal vessel involvement more commonly demonstrated elevated PPs, whereas patients with narrowed PPs were more likely to have periaortic hematoma and/or pericardial effusion. Narrowed PPs were also correlated with greater incidences of hypotension, cardiac tamponade, and mortality. Patients with TAAAD who were managed with endovascular and hybrid procedures and those with renal failure tended to have markedly elevated PPs. No difference in aortic regurgitation at presentation was noted among groups. In conclusion, patients with TAAAD in the third PP quartile had better in-hospital outcomes than patients in the lowest quartile. Patients with narrowed PPs experienced more cardiac complications, particularly cardiac tamponade, whereas those with markedly elevated PPs were more likely to have abdominal aortic involvement. Presenting PP offers a clue to different manifestations of acute aortic dissection that may facilitate initial triage and care. © 2014 Elsevier Inc. All rights reserved. **(Am J Cardiol 2014;113:1255–1259)**

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See page 1258 for disclosure information.

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Pulse pressure (PP) has been the focus of a number of studies in several populations of cardiovascular disease.[1,2] PP, the force that a heart generates with each contraction, is defined as the difference between systolic and diastolic blood pressure. Wide PP is strongly correlated with long standing hypertension where there is a loss of aortic elasticity in chronic disease.[3,4] Wide PP has been associated with cardiovascular, coronary, and all-cause mortality in various patient populations.[5–9] A narrow PP at hospital admission is an independent predictor of mortality in patients with acute coronary syndrome.[10] Little is known about the relation between PP and type A acute aortic dissection (TAAAD). We hypothesized that patients with TAAAD who presented with a narrow PP would be more likely to have cardiac tamponade and experience negative outcomes and increased mortality compared with patients who exhibited normal and mildly elevated PPs.[11] We also believe that patients with a wide PP might have increased age, more malperfusion, or aortic valve disruption leading to aortic valve regurgitation and worse outcomes.

Methods

The International Registry of Acute Aortic Dissection (IRAD) has collected data on patients with acute aortic dissection at 24 aortic referral centers in 11 countries since

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Table 1
Demographics and patient history for all patients with type A aortic dissection

Variable	PP (mm Hg)				p Value
	≤39	40–56	57–75	≥76	
Number of patients	430 (21.9)	554 (28.2)	490 (25.0)	486 (24.8)	—
Demographics					
Age (yrs)	63.6 ± 13.477	62.04 ± 14.848	59.74 ± 14.794	60.78 ± 13.640	<0.001*
Age (≥70 yrs)	147 (34.2)	183 (33.0)	124 (25.3)	134 (27.6)	0.006*
Men	276 (64.2)	361 (65.2)	339 (69.2)	357 (73.5)	0.008*
White	376 (91.7)	468 (90.0)	404 (87.4)	378 (84.6)	0.006*
History					
Hypertension	301 (71.7)	382 (69.8)	350 (72.5)	385 (79.9)	0.002*
Atherosclerosis	94 (22.7)	106 (19.8)	83 (17.5)	104 (21.7)	0.224
The Marfan syndrome	13 (3.1)	31 (5.7)	30 (6.2)	14 (2.9)	0.021
Bicuspid aortic valve	17 (4.6)	20 (4.3)	16 (3.9)	15 (3.7)	0.924
Other aortic disease	9 (2.1)	8 (1.5)	8 (1.7)	6 (1.3)	0.756
Smoker: current	34 (28.3)	54 (36.2)	46 (32.4)	54 (37.2)	0.409
Cocaine abuse	4 (1.0)	8 (1.5)	8 (1.7)	9 (1.9)	0.702
Family history of aortic disease	9 (6.2)	17 (9.2)	23 (14.3)	10 (6.1)	0.036
Known aortic aneurysm	50 (12.1)	73 (13.5)	54 (11.3)	49 (10.2)	0.403
Previous aortic dissection	13 (3.1)	20 (3.7)	22 (4.6)	19 (4.0)	0.704
Aortic aneurysm/dissection surgery	22 (5.2)	37 (6.9)	30 (6.3)	31 (6.5)	0.742
Previous cardiac surgery	41 (9.7)	69 (12.9)	58 (12.3)	69 (14.4)	0.191

Data are presented as mean ± SD or n (%).
* Variables that have both a p value of <0.05 and a linear-by-linear association of <0.05.

Table 2
Findings on diagnostic imaging for all patients with type A aortic dissection

Variable	PP (mm Hg)				p Value
	≤39	40–56	57–75	≥76	
True intramural hematoma on first imaging study	21 (5.3)	26 (5.1)	17 (3.7)	17 (3.9)	0.567
True intramural hematoma progressing to dissection	4 (19.0)	4 (16.0)	3 (17.6)	2 (14.3)	1.000
Intramural hematoma (any study)	81 (18.8)	112 (20.2)	84 (17.1)	76 (15.6)	0.248
Pre-/postoperative extension of dissection	38 (9.4)	40 (7.7)	34 (7.3)	35 (7.6)	0.679
Any aneurysm	198 (51.0)	259 (51.8)	230 (51.3)	220 (50.2)	0.971
False lumen patency					
Patent	193 (72.3)	272 (71.0)	222 (73.3)	228 (71.0)	0.905
Partial thrombosis	44 (16.5)	66 (17.2)	61 (20.1)	67 (20.9)	0.423
Complete thrombosis	30 (11.2)	45 (11.7)	20 (6.6)	26 (8.1)	0.075
Abdominal vessel involvement	94 (22.1)	95 (17.3)	101 (20.8)	133 (27.6)	0.001*
Right renal	26 (6.1)	35 (6.4)	36 (7.4)	45 (9.3)	0.206
Left renal	56 (13.1)	48 (8.7)	59 (12.1)	85 (17.6)	<0.001*
Distal communication	69 (27.2)	92 (26.3)	73 (26.7)	83 (28.8)	0.906
Arch vessel involvement	147 (46.2)	166 (39.2)	128 (37.0)	135 (37.2)	0.052
Coronary artery compromised	32 (9.9)	53 (12.8)	35 (10.2)	48 (13.6)	0.337

Data are presented as n (%).
* Variables that have both a p value of <0.05 and a linear-by-linear association of <0.05.

January 1, 1996. Patients are enrolled if they present with nontraumatic, spontaneous, or iatrogenic dissections within 14 days of symptom onset. They are identified prospectively by physicians or retrospectively through discharge diagnoses, imaging, and/or surgical databases. Diagnosis is based on symptom onset, patient history, imaging, surgical examination, and/or autopsy. All sites have received approval from each hospital's institutional review board to participate in IRAD. A comprehensive description of the organization and methods of the IRAD database have been detailed previously.[12]

A standardized form with 290 variables was used to record information on patient demographics, medical history, clinical presentation, physical findings, imaging study results, medical and interventional management, and in-hospital outcomes. Data were collected at presentation or retrospectively through medical record analysis and reviewed for face validity and completeness at the coordinating center at the University of Michigan.

This study included patients with TAAAD enrolled in IRAD from January 1, 1996 to July 26, 2012. Patients with type B dissections and/or iatrogenic dissections were excluded, resulting in 1,960 study patients. These patients were arranged into quartiles based on PP at hospital presentation: narrow (≤39 mm Hg, n = 430), normal (40 to 56 mm

Table 3
Management, in-hospital pre- and/or postoperative complications, and mortality for all patients with type A aortic dissection

Variable	PP (mm Hg)				p Value
	≤39	40–56	57–75	≥76	
Management					
Medical	51 (11.9)	75 (13.5)	54 (11.0)	57 (11.7)	0.642
Surgical	372 (86.5)	475 (85.7)	426 (87.1)	410 (84.4)	0.639
Endovascular	4 (0.9)	1 (0.2)	7 (1.4)	9 (1.9)	0.031*
Hybrid	3 (0.7)	3 (0.5)	2 (0.4)	10 (2.1)	0.047*
Complications					
Aortic regurgitation	194 (55.1)	239 (51.3)	231 (57.5)	241 (57.5)	0.139
Periaortic hematoma	105 (30.2)	93 (20.2)	70 (17.9)	70 (17.7)	<0.001*
Pericardial effusion	224 (58.8)	235 (47.2)	153 (35.1)	138 (32.2)	<0.001*
Cerebrovascular accident: 1-h outcome	41 (10.5)	43 (8.7)	36 (8.1)	41 (9.3)	0.653
Coma: 1-h outcome	8 (2.1)	14 (2.8)	6 (1.4)	9 (2.1)	0.478
Spinal cord ischemia	4 (1.0)	4 (0.8)	4 (0.9)	4 (0.9)	0.986
Myocardial ischemia	51 (12.4)	61 (11.6)	53 (11.3)	35 (11.3)	0.078
Myocardial infarction	33 (8.0)	33 (6.3)	29 (6.2)	20 (4.3)	0.152
Mesenteric ischemia/infarction	25 (6.1)	30 (5.7)	19 (4.1)	36 (7.7)	0.126
Pre-/postoperative renal failure	102 (24.9)	141 (26.7)	94 (20.1)	136 (29.1)	0.014*
Pre-/postoperative extension of dissection	38 (9.4)	40 (7.7)	34 (7.3)	35 (7.6)	0.680
Pre-/postoperative hypotension	223 (53.9)	171 (32.4)	79 (17.0)	77 (16.6)	<0.001*
Cardiac tamponade	32 (7.5)	17 (3.1)	0 (0.0)	3 (0.6)	<0.001*
Limb ischemia	56 (13.8)	56 (10.7)	57 (12.2)	74 (15.9)	0.097
Complications (any)	34 (8.0)	33 (6.0)	27 (5.6)	44 (9.1)	0.099
In-hospital mortality	133 (30.9)	141 (25.5)	80 (16.3)	114 (23.5)	<0.001*
Cause of death: aortic rupture	23 (26.7)	27 (29.7)	16 (29.1)	15 (21.7)	0.700
5-yr Kaplan-Meier survival estimates (n at risk)	77.7 (19)	81.0 (21)	84.5 (19)	84.2 (16)	0.507

Data are presented as n (%).
* Variables that have both a p value of <0.05 and a linear-by-linear association of <0.05.

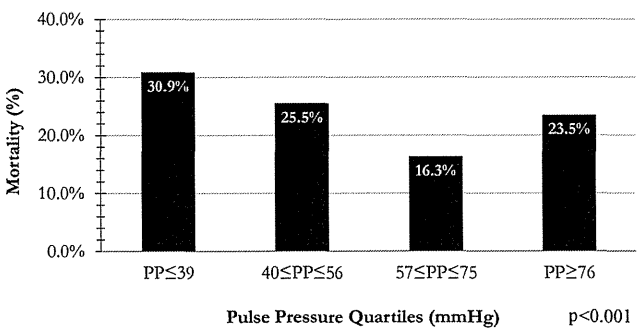

Figure 1. In-hospital mortality (%) among patients with acute type A aortic dissection in narrow, normal, mildly elevated, and markedly elevated PP quartiles.

Hg, n = 554), mildly elevated (57 to 75 mm Hg, n = 490), and markedly elevated (≥76 mm Hg, n = 486). When patients fell between quartiles, they were assigned to the higher grouping resulting in a slightly uneven sample size between quartiles.

Categorical variables were compared across PP quartiles using Pearson's chi-square test or Fisher's exact test as appropriate. Continuous variables were examined using analysis of variance. Linear-by-linear association was used to study linear trends across quartiles. The tables are marked with an asterisk to indicate variables that have both a p value of <0.05 and a linear-by-linear association of <0.05. Variables detailing demographics, patient history, presentation, imaging results, complications, and outcomes were analyzed for their relation to PP in patients with TAAAD. All statistical analyses were performed using SPSS, version 20.0 (IBM Corp.).

Results

The study cohort consisted of 1,960 subjects with TAAAD including 21.9% of patients in the narrow quartile, 28.3% in the normal quartile, 25.0% in the mildly elevated quartile, and 24.8% in the markedly elevated quartile. Patients in the narrow quartile (PP ≤39 mm Hg) were typically aged >70 years, women, a race other than Caucasian, and had an average age of 63.6 years (Table 1). Patients in the markedly elevated quartile (PP ≥76 mm Hg) had an average age of 60.8 years and tended to be Caucasian, men, and have a history of hypertension (Table 1). There was no correlation seen between PP and a history of atherosclerosis, previous smoking, or any previously diagnosed aortic conditions (Table 1).

Patients who presented with a narrow PP tended to have more cardiac complications in comparison with those in the other 3 quartiles (Tables 2 and 3). Specifically, they had greater incidences of periaortic hematoma, pericardial effusion, and cardiac tamponade than patients with normal, mildly elevated, and markedly elevated PPs (Table 3). Patients with TAAAD in the narrow PP quartile had a greater risk of in-hospital mortality than patients in the other quartiles (Figure 1). There was no relation between narrow PP and false lumen patency, coronary artery compromise, or long-term mortality (Tables 2 and 3).

Patients with TAAAD who had markedly elevated PPs at presentation were more inclined to have abdominal aorta involvement and distal complications compared with patients with narrow, normal, and mildly elevated PPs (Tables 2 and 3). These patients had greater incidences of abdominal vessel involvement, left renal artery involvement, and in-hospital renal failure than patients in the other 3 quartiles (Table 2). The selection of endovascular and hybrid managements was also correlated with wide PP at presentation (Table 3). There was no link between wide PP and aortic regurgitation, right renal involvement, or distal communication (Tables 2 and 3).

Discussion

This is the first comprehensive assessment of the association of presenting PP with in-hospital complications and mortality of patients with acute type A aortic dissection. As expected, the quartile with the narrowest PPs ($\leq$39 mm Hg) had the highest mortality rate (30.9%). This subgroup was characterized by a high incidence of pericardial effusion and hypotension. Such patients typically have pericardial bleeding as a result of leakage from the tear in the aortic wall into the pericardial sac's reflection, which extends up into the ascending aorta. This often leads to early death, but for a percentage of patients, the leakage is modest at first, leading to hemodynamic blunting of cardiac systolic function but not frank tamponade.

We had also hypothesized that patients in the markedly elevated PP quartile would have increased mortality compared with those in the middle 2 quartiles owing to several other factors. We believed that wider PPs would be seen more often in patients with greater underlying aortic stiffness, loss of peripheral resistance owing to malperfusion or extensive dissection, and/or possibly due to development of aortic valve regurgitation in a subset of patients. Also, because PP widens with age, we expected that older patients would be found in the markedly elevated PP quartile. Interestingly, the quartile with widest PP did not have the highest average age, but it did contain the greatest number of men (73.5% compared with 64.2% in quartile 1). Expectedly, this group experienced higher rates of abdominal artery involvement, renal artery compromise, and renal failure. We believe that such malperfusion syndromes are associated with release of various cytokines, which lower peripheral arterial resistance and accordingly elevate PP in affected patients. This association could influence therapeutic approaches including site of aortic access for endovascular therapy (e.g., axillary artery vs femoral artery). No association between wider PPs and aortic valve insufficiency was found. This likely relates to the notion that a lowering of peripheral arterial resistance and therefore diastolic blood pressure represents an adaptation to chronic aortic valve regurgitation but not acute aortic valve incompetence.

A high PP has been linked to cardiovascular risk in a number of populations. The Framingham Study discovered that elevated PP is an important risk predictor for cardiovascular events in patients living in Massachusetts.[13] Similarly, Benetos et al[14] showed that PP elevation predicts increased cardiovascular risk in a cohort of French men. Domanski et al[7] showed that elevated PP provided independent risk predictability for cardiovascular events over 16.5 years in a cohort of subjects enrolled in the National Health and Nutrition Examination Survey registry. Zakopoulos et al[15] observed that a widened PP predicted elevated cardiovascular risk even in normotensive subjects. PP appears to be a better predictor of myocardial infarction,[5] left ventricular hypertrophy,[5] and cardiovascular death [4,5,16] than either diastolic or systolic blood pressure alone.

Each of these associations underlines the general notion that PP reflects 2 mechanisms of cardiovascular physiology, which are strongly correlated with end organ risk.[1,2] The first is development of a high-pressure aortic wave by the left ventricle (proximal compartment) leading to the recorded systolic pressure. Left ventricular hypertrophy is more common in patients with widened PP and, of course, such hypertrophy correlates with long-term risk of heart failure, both diastolic and systolic. The second association is indirect and relates to the distal compartment of arterial function. As arteries stiffen and lose their natural elasticity, diastolic blood pressure decreases, again leading to a widened PP. Thus, both cardiac and arterial physiologies are tightly connected over time as recorded through serial measurement of PP.

Our data suggest that in addition to frank hypotension, a narrow PP indicates a high likelihood of pericardial involvement, and a narrow PP should compel the care team to arrange for the most expeditious aortic repair possible. Second, clinicians should also glean from our study that a markedly elevated pulse may be associated with malperfusion conditions affecting the mesentery, renal bed, limbs, or other vital structures.

There are several limitations to our study. First, we analyzed blood pressure and its associated PP at a single point in time, the first recorded measurement. This ignores the notion that PP is a dynamic measurement, varying beat by beat. Second, our associations of PP with patient outcomes have excluded the effects of diagnostic testing, medical treatment, surgical treatment, and complications. However, overall treatment (surgery in approximately 85%) was relatively similar across all 4 quartiles.

Disclosures

The authors have no conflicts of interest to disclose.

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Stroke and Outcomes in Patients With Acute Type A Aortic Dissection

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Stroke and Outcomes in Patients With Acute Type A Aortic Dissection

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Background—Stroke is a highly dreaded complication of type A acute aortic dissection (TAAAD). However, little data exist on its incidence and association with prognosis.

Methods and Results—We evaluated 2202 patients with TAAAD (mean age 62±14 years, 1487 [67.5%] men) from the International Registry of Acute Aortic Dissection to determine the incidence and prognostic impact of stroke in TAAAD. Stroke was present at arrival in 132 (6.0%) patients with TAAAD. These patients were older (65±12 versus 62±15 years; P=0.002) and more likely to have hypertension (86% versus 71%; P=0.001) or atherosclerosis (29% versus 22%; P=0.04) than patients without stroke. Chest pain at arrival was less common in patients with stroke (70% versus 82%; P<0.001), and patients with stroke presented more often with syncope (44% versus 15%; P<0.001), shock (14% versus 7%; P=0.005), or pulse deficit (51% versus 29%; P≤0.001). Arch vessel involvement was more frequent among patients with stroke (68% versus 37%; P<0.001). They had less surgical management (74% versus 85%; P<0.001). Hospital stay was significantly longer in patients with stroke (median 17.9 versus 13.3 days; P<0.001). In-hospital complications, such as hypotension, coma, and malperfusion syndromes, and in-hospital mortality (adjusted odds ratio, 1.62; 95% confidence interval, 0.99–2.65) were higher among patients with stroke. Among hospital survivors, follow-up mortality was similar between groups (adjusted hazard ratio, 1.15; 95% confidence interval, 0.46–2.89).

Conclusions—Stroke occurred in >1 of 20 patients with TAAAD and was associated with increased in-hospital morbidity but not long-term mortality. Whether aggressive early invasive interventions will reduce negative outcomes remains to be evaluated in future studies. ***(Circulation.* 2013;128[suppl 1]:S175-S179.)**

Key Words: aortic dissection ■ mortality ■ stroke management

Stroke is a highly dreaded complication of type A acute aortic dissection (TAAAD). Brain tissue ischemia from hypotension and direct compromise of cerebral circulation are believed to be the underlying mechanisms of stroke in patients with TAAAD.[1] Single-center studies of few patients have reported a stroke incidence between 3% and 32% and demonstrated increased morbidity and mortality in these patients.[2–5] Accordingly, we evaluated a large cohort of >2000 patients with TAAAD enrolled in the International Registry of Acute Aortic Dissection (IRAD)[6–8] to determine the incidence, presentation, management, prognosis, and outcomes of stroke in this cohort.

Methods

Study Population

We analyzed data on 2202 TAAAD IRAD patients enrolled from January 1, 1996, to August 18, 2012, at 25 aortic centers. The structure and methods of IRAD have been previously published.[6–8] Patients were identified prospectively at presentation and retrospectively via discharge diagnoses, imaging, and hospital databases. Diagnosis was confirmed by imaging, surgical visualization, or autopsy. Each site's institutional review committee approved participation.

Data Collection and Definitions

Data on 290 variables were recorded on a standardized form detailing demographics, history, clinical presentations, imaging results,

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