UNIVERSIDADE DA CORUÑA

“Epidemiology of acute traumatic aortic injuries in Galicia, Spain. Development and validation of a score for early diagnosis of aortic injuries in major blunt chest trauma patients and optimization of management algorithm”

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This thesis has been submitted to the *Universidad de A Coruña* in fulfilment of the requirements for the degree of “*Doctor con Mención Internacional*” by the *Universidad de A Coruña.*

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CERTIFICAN:

Que el trabajo contenido en la presente memoria y titulado:

"Epidemiología de las lesiones traumáticas agudas en Galicia. Desarrollo y validación de un método diagnóstico precoz de lesión aórtica en los pacientes con traumatismo torácico cerrado mayor y optimización de las estrategias de manejo"

"Epidemiology of acute traumatic aortic injuries in Galicia, Spain. Development and validation of a score for early diagnosis of aortic injuries in major blunt chest trauma patients and optimization of management algorithm"

Que para optar al grado de Doctor con "Mención Internacional" presenta D. Víctor Xesús Mosquera Rodríguez, licenciado en Medicina y Cirugía, ha sido realizado bajo nuestra dirección y reúne las características precisas para su presentación y defensa como Tesis Doctoral.

A Coruña, 5 de Marzo de 2012

Fdo. Javier Muñiz García **Fdo. Milagros Marini Díaz** **Fdo. José María Herrera Noreña**

DEDICATION

"This Thesis is dedicated to the loving memory of my sister, Bea. Gone, but not forgotten"

DECLARATION

I hereby declare that the work presented in this thesis is my own, except where stated.

This work has not been submitted for any other degree or professional qualification.

Victor X. Mosquera Rodríguez

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LIST OF ABBREVIATIONS (in alphabetical order)

- **AIS:** Abbreviated Injury Scale.
- **ATAI(s):** Acute Traumatic Aortic Injury(ies).
- **AUC:** Area Under the Curve.
- **AVP:** Auto vs. Pedestrian.
- **CHUAC:** *Complejo Hospitalario Universitario de A Coruña.*
- **CHUS:** *Complejo Hospitalario Universitario de Santiago de Compostela.*
- **CHUVI:** *Complejo Hospitalario Universitario de Vigo.*
- **CI:** Confidence interval.
- **CPB:** Cardiopulmonary Bypass.
- **CPK:** Creatine Phosphokinase.
- **CSF:** Cerebrospinal Fluid.
- **CXR:** Chest X-Ray.
- **DSA:** Digital Subtraction Angiography.
- **ER:** Emergency.
- **Gy:** Grays.
- **HCA:** Hypothermic Circulatory Arrest.

- **HR:** Hazard Ratio.
- **ICU:** Intensive Care Unit.
- **ISS:** Injury Severity Score.
- **IVUS:** Intravascular Ultrasound.
- **LHB:** Left Heart Bypass.
- **LMW:** Left Mediastinal Width.
- **LSA:** Left Subclavian Artery.
- **MAAVB(s):** Major Aortic Abdominal Visceral Branch(es).
- **MAP:** Mean Arterial Pressure.
- **MAI:** Minimal Aortic Injuries.
- **MCC:** Motorcycle Collision.
- **MDCT:** Multidetector Computed Tomography.
- **MW:** Mediastinal Width.
- **MWR:** Mediastinal Width Ratio.
- **MPR:** Multiplanar reconstructions.
- **mSv:** milisieverts.
- **MVC:** motor vehicle collisions.
- **OR:** Odds Ratio.

- **ROC:** Receiver Operating Characteristic.
- **RTS:** Revised Trauma Score.
- **SAI:** Significant Aortic Injuries.
- **SCI:** Spinal Cord Ischemia.
- **Sv:** Sieverts.
- **TEE:** Transesophageal Echocardiography.
- **TEVAR:** Thoracic Endovascular Aortic Repair.
- **TDMAC:** Tridodecylmethylammonium Chloride.
- **TRISS:** Trauma Injury Severity Score.
- **YPLL:** Years of Productive Life Lost

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- Víctor X Mosquera, Milagros Marini, Javier Muñiz, Vanesa Asorey-Veiga, Belen Adrio-Nazar, Jose M Herrera, Gonzalo Pradas-Montilla, and Jose J Cuenca. Blunt traumatic aortic injuries of the ascending aorta and aortic arch: a clinical multicentre study. *Submitted to*: *Injury. Under Review.* JINJ-D-12-00337

SUMMARY

Acute traumatic aortic injury (ATAI) usually occurs in patients with major blunt chest trauma and has devastating consequences. An early diagnosis with risk stratification, control of blood pressure and cardiac contractility is the cornerstone of the approach to aortic injuries in these patients.

Optimization of diagnostic resources and a specific management is mandatory to both prevent potentially lethal aortic-related complications in high-risk major trauma patients, and to avoid unnecessary costs and radiation exposure in low-risk trauma patients.

This thesis describes two clinical studies designed to characterise the epidemiology and clinical profile of major trauma patients with ATAI among overall major blunt chest trauma patients in our Spanish region, Galicia, whose population is more than 2,700,000 inhabitants, and to develop and further validate a predictive score of the probability of presenting an ATAI in major trauma patients, which was named *Traumatic Aortic Injury Score* (*TRAINS*).

In the first instance a retrospective descriptive study was undertaken in all major trauma patients with blunt chest trauma admitted to a public hospital in Galicia from 2006 to 2010 (1,760 patients), followed by a comparison of the distinct clinical profile between trauma patients with (44 patients) and without an associated ATAI (1,716 patients).

This epidemiological part of the research showed that overall importance in terms of percentage of ATAIs among major trauma patients with blunt chest trauma between 2006 and 2010 in our institution and region was 4.4% and 2.5% respectively. Likewise, the yearly proportion of ATAIs among major trauma patients in Galicia was 1.1%-

3.3%, whereas it ranged from 2.5% to 7.8% in our institution. After estimation of the number of major trauma patients with ATAI who die at the site of accident or during transportation, the actual resulting incidence of ATAI in Galicia would be 3 to 6.1 cases per 100,000 inhabitants per year.

Our research confirmed that in Galicia major trauma patients with associated ATAIs present a different epidemiological profile, prognosis, initial clinical presentation and the number and distribution of associated injuries. While major trauma patients without aortic injury distribute fairly homogeneously through the whole age span, ATAIs concentrate among 16 to 35 years old trauma patients, where 54.6% of overall ATAI occurs. The motor vehicle collision is the commonest cause of accident among ATAI victims in Galicia, but we have found a higher proportion of motorcycle collisions, falls and crush traumas and a lower proportion of auto-pedestrian accidents among patients with ATAI compared to those reported in ATAI victims by other authors. The proportion of "atypical or non-isthmal" aortic injuries (43.2%) is significantly higher than the 7% to 15% reported in other clinical series, also highlighting a remarkably higher proportion of injuries at the aortic arch (25%). Major trauma patients with ATAIs presented with haemodynamic instability on admission more frequently than major trauma patients without aortic injury, and they also had a higher proportion of severe extra-thoracic injuries, which justify their worse prognosis.

The second part of the research was a cross-sectional study of a diagnostic procedure. The development of a predictive score for the risk of ATAI in major trauma patients with blunt chest trauma was carried out in two stages. In the first stage, we analysed the clinical and radiological characteristics of major blunt chest trauma patients in order to develop the screening tool for ATAIs among major trauma patients. In the second stage, we validated the predictive score in an independent external population of major trauma patients. In the predictive score development, the overall study population consisted of 640 major trauma patients (all of them with blunt chest trauma) divided into two datasets: a score dataset provided only by the *Complejo Hospitalario Universitario de A Coruña* (76 consecutive major trauma patients with ATAI and 304 without aortic injury), and an independent validation dataset provided by other three different institutions: *Complejo Hospitalario Universitario de Vigo*, *Complejo Hospitalario Universitario de Santiago de Compostela*, and *Hospital Clínic Universitari de Valencia* (52 consecutive major trauma patients with ATAI and 208 without aortic injury).

Bivariate analysis identified variables of potential influence in presenting aortic injury among major blunt chest trauma patients. Subsequently, confirmed variables by stepwise forward logistic regression were assigned a score according to their corresponding beta coefficient which was rounded to the closest integer value (1-4).

The predictors of aortic injury that we identified included: widened mediastinum (OR: 30.82; CI: 12.05-78.81); hypotension <90 mmHg (OR: 5.85; CI: 2.26-15.15); long bone fracture (OR: 8.60; CI: 2.15-34.31); pulmonary contusion (OR: 4.12; CI: 1.11-15.20); left scapula fracture (OR: 3.81; CI: 1.24-11.69); hemothorax (OR: 3.47; CI: 1.19-10.09), and pelvic fracture (OR: 2.96; CI: 1.15-7.60).

We developed a contemporaneous multivariate prediction model for traumatic aortic injury after major trauma with a sensitivity >93% and a specificity >85%. The small number of ATAI patients who were misdiagnosed by *TRAINS* (false negatives) presented low-degree aortic injuries. The scoring method also proved its accuracy in both an internal and an external validation process. The *TRAINS* demonstrated its ability to diagnose ATAIs among major trauma patients with a sensitivity >92% and a specificity >85% in a current multicentre population of major trauma patients, thus confirming its applicability at the current time and in different geographical areas.

We demonstrated that the conventional trauma risk scores fail to show statistical relationship between the severity of the trauma and the degree of severity of the aortic injury. Thus, the conventional trauma severity scores are useless to cast suspicion on the diagnosis of ATAI. On the contrary, *TRAINS* score has proven to be related with the severity of the aortic injury and to be useful even in the diagnosis of low-degree ATAI.

In summary, the *TRAINS* and associated algorithm have been designed to be used in daily practice to easily and rapidly identify major trauma patients who are at risk of aortic injury, thus avoiding unnecessary costs and radiation exposure in low-risk trauma patients. On the other hand, the *TRAINS* may raise suspicion of ATAI even in the cases of low-degree aortic injuries, which require a close imaging surveillance to determine whether or not those patients will need a further intervention. The *TRAINS* algorithm is also useful for resource allocation planning, enabling clinicians to refer patients at high risk of traumatic aortic injuries to specialized units, providing the ability to rapidly diagnose and therapeutically manage this critical subset of trauma patients in order to avoid potentially lethal aortic-related complications.

EXTENDED SUMMARY IN SPANISH (RESÚMEN EXTENDIDO EN ESPAÑOL)

• Introducción

Los pacientes con traumatismos mayores cerrados de tórax pueden presentar lesiones traumáticas de aorta, las cuales conducen frecuentemente a complicaciones cardiovasculares potencialmente letales. Las lesiones traumáticas de aorta son la segunda causa de mortalidad en los pacientes politraumatizados, únicamente superadas por las lesiones neurológicas. Además, constituyen una importante fuente de morbilidad y de consumo de recursos sanitarios y sociales tanto en términos de años de vida productivos perdidos como de costes por dependencia de los pacientes supervivientes.

Los accidentes de tráfico son la principal causa de lesiones traumáticas de aorta, seguidos por las precipitaciones, los atropellos y, en último lugar, los traumatismo sin deceleración o traumatismos de "baja velocidad" como los aplastamientos. Los datos internacionales de los que disponemos cifran la proporción de lesiones traumáticas de aorta entre el 0.5% y el 2% del total de accidentes de tráfico no letales y entre el 10%-20% de todas los fallecimientos por accidentes de tráfico. Sin embargo, no existen datos publicados que cifren su proporción entre los pacientes traumatizados en España y, concretamente, en Galicia.

En general, las lesiones traumáticas de aorta se pueden clasificar en tres categorías en cuanto a su pronóstico a corto plazo. El grupo más amplio con el 70%-80% de los pacientes engloba a las víctimas fallecidas en el lugar de accidente, que suelen presentar una rotura completa no contenida de las tres capas de pared aórtica que conduce a una rápida exanguinación de la víctima. La segunda categoría incluye entre el 2% y el 5% de los pacientes con lesión traumática de aorta, que son aquellos que llegan inestables al hospital o mueren durante el trasporte al centro hospitalario. La mortalidad global en este segundo grupo excede el 90%. Finalmente, hay un porcentaje de pacientes entre el 20% y el 25%, que permanecen hemodinámicamente estables desde el punto de vista de la lesión aórtica y que presentan una mortalidad intrahospitalaria global alrededor del 25%, fundamentalmente por lesiones traumáticas asociadas no aórticas.

El manejo del paciente con traumatismo torácico mayor y lesión aórtica asociada ha cambiado sustancialmente en la última década gracias a la expansión de técnicas de imagen de alta resolución como la tomografía computerizada multidetector, a la expansión de las técnicas endovasculares para el tratamiento de las lesiones aórticas, y a la institución del tratamiento quirúrgico diferido tras la estabilización de otras lesiones traumáticas no aórticas. Sin embargo, un diagnóstico precoz con estratificación del riesgo de complicación aórtica, junto con un control óptimo de la presión arterial y de la contractilidad cardiaca mediante betabloqueantes, siguen siendo la piedra angular del manejo de este subgrupo crítico de pacientes con traumatismo torácico mayor. Por otra parte, la optimización de los recursos diagnósticos y la instauración de un manejo específico no sólo son fundamentales para prevenir complicaciones cardiovasculares en pacientes con alto riesgo de lesión aórtica, si no también para evitar el sobreuso de los recursos hospitalarios con costes económicos y exposición a radiaciones ionizantes innecesarios en los pacientes politraumatizados con bajo riesgo de lesión aórtica. Un paciente joven politraumatizado estándar que recibe más de dos pruebas de imagen de alta resolución con exposición a radiación ionizante incurre en un incremento del riesgo acumulado de desarrollar algún tipo de neoplasia durante su vida.

- **Objetivos**

Esta tesis consta de dos estudios clínicos diferentes desarrollados para cumplir dos objetivos independientes: I-Describir la epidemiología y definir el perfil clínico característico del paciente con traumatismo torácico mayor cerrado con lesión traumática de aorta con respecto al resto de pacientes con traumatismos mayores cerrados de tórax sin lesión aórtica asociada en nuestro área comunitaria, es decir, en Galicia; II-Desarrollar y posteriormente validar un sistema de puntuación para determinar la probabilidad de que un paciente con traumatismo torácico cerrado mayor presente una lesión traumática aórtica asociada. Dicho sistema de puntuación se ha denominado *TRaumatic Aortic INjury Score* (*TRAINS*).

- **Metodología**

Para efectos del estudio y de acuerdo a la literatura internacional, se ha definido paciente con traumatismo torácico mayor como aquel paciente con traumatismo torácico que presenta una puntuación *Injury Severity Score* mayor de 15 puntos en el momento de admisión hospitalaria. Asimismo, se ha empleado la clasificación de severidad de la lesión traumática aórtica en cuatro grados (I a IV) admitida internacionalmente.

Para alcanzar el primer objetivo (I- Epidemiología de la lesión traumática aórtica en Galicia) se desarrolló un estudio descriptivo retrospectivo que englobó a todos los pacientes con traumatismo torácico cerrado mayor admitidos en un hospital público en Galicia desde el año 2006 al año 2010, esto es 1,760 pacientes consecutivos, seguido de un análisis bivariable comparativo de las distintas características epidemiológicas y clínicas entre aquellos pacientes con lesión traumática de aorta asociada (44 pacientes) y el resto de pacientes con traumatismo torácico cerrado mayor sin lesión aórtica (1,716 pacientes).

En la consecución del segundo objetivo (II- escala predictiva de riesgo de lesión traumática aórtica), el desarrollo del método predictivo del riesgo de lesión traumática de aorta en los pacientes con traumatismo torácico cerrado mayor se realizó a su vez en dos fases. En la primera fase, se elaboró un método predictivo para la clasificación de los pacientes traumatizados en función de su probabilidad de presentar una lesión traumática de aorta, mientras que en la segunda fase se efectuó una validación tanto interna como externa del método predictivo de riesgo obtenido en la primera fase.

En el desarrollo de la investigación para lograr el segundo objetivo (método predictivo y validación), la población global incluida fue de 640 pacientes con traumatismo torácico cerrado mayor divididos en dos muestras: una muestra empleada exclusivamente en el desarrollo de la escala de riesgo, que englobó únicamente pacientes procedentes del *Complejo Hospitalario Universitario de A Coruña* (76 pacientes con traumatismo torácico cerrado mayor con lesión traumática de aorta y 304 sin lesión aórtica asociada); y una muestra totalmente independiente de validación externa proporcionada por otras 3 instituciones diferentes (*Complejo Hospitalario Universitario de Vigo*, *Complejo Hospitalario Universitario de Santiago de Compostela*, y *Hospital Clínic Universitari de Valencia*), que incorporó 260 enfermos (52 pacientes con traumatismo torácico cerrado mayor con lesión traumática de aorta y 208 sin lesión aórtica asociada).

En la primera fase de elaboración del método predictivo se efectuó un análisis bivariable de las características clínicas y de la radiología simple de tórax para identificar variables potencialmente influyentes en la probabilidad de presentar una lesión traumática de aorta. Las variables identificadas como predictores potenciales de la presencia de lesión traumática de aorta en pacientes con traumatismo torácico cerrado mayor se introdujeron en un modelo de regresión logística binaria condicional hacia delante para confirmar las variables verdaderamente predictivas. Dichas variables confirmadas por el análisis de regresión logística binaria recibieron una puntuación de 1 a 4 puntos de acuerdo a su coeficiente beta, el cual se redondeó al número entero más próximo.

El área bajo la curva de Característica Operativa del Receptor (COR) se utilizó para medir el “poder de discriminación” de la prueba o grado en que el modelo distingue entre individuos en los que ocurre el evento y los que no.

El test de Hosmer-Lemeshow se empleó para evaluar la bondad de ajuste del modelo de regresión logística y medir la “calibración” o grado en que la probabilidad predicha coincide con la observada.

En la segunda fase, o fase de validación del método predictivo, se efectuó una doble validación de la técnica. En primer lugar, se empleó la técnica simple de *Bootstrap*, que proporciona estimaciones del error estadístico, para realizar una validación interna mediante la obtención de 1,000 sub-muestras distintas de los 380 pacientes de la muestra de elaboración de la escala predictiva. Se analizaron los coeficientes de regresión y los errores estándar obtenidos en las 1,000 sub-muestras. A continuación, se llevó a cabo un procedimiento de validación externa empleando los 260 pacientes de la muestra de validación procedente de los otros tres centros independientes.

- **Resultados**

El análisis bivariable identificó 18 variables como predictores potenciales de la presencia de lesión traumática de aorta en pacientes con traumatismo torácico cerrado mayor. Sin embargo, el análisis de regresión logística binaria confirmó únicamente siete de esas variables como factores de riesgo para la presencia de lesión traumática de aorta, las cuales recibieron una puntuación de 1 a 4 puntos de acuerdo a su coeficiente beta proporcionado por el análisis de regresión: ensanchamiento mediastínico en radiografía de tórax, 4 puntos; hipotensión <90 mmHg, 2 puntos; fractura de huesos largos, 2 puntos; contusión pulmonar, 1 punto; fractura de escápula izquierda, 1 punto; hemotórax, 1 punto; y fractura pélvica, 1 punto. De esta forma, la escala *TRAINS* resultante podría presentar una puntuación entera entre 0 y 12 puntos. El área bajo la curva COR obtenida con el método *TRAINS* fue de 0.96 (0.95-0.98). El test de Hosmer-Lemeshow no fue estadísticamente significativo (Valor Chi cuadrado= 13.14, *P*=0.10), lo que indicó una excelente calibración del método predictivo.

Se escogió un valor de corte de la escala ≥4 puntos para considerar positiva la prueba y maximizar tanto la sensibilidad como la especificidad. Dicho valor de corte proporcionó unos valores de sensibilidad del 93.42% (87.19%-99.65%) y especificidad del 85.85% (81.77%-89.94%). El índice de Youden para una puntuación ≥4 puntos fue de 0.79 (0.72-0.86), mientras que la razón de verosimilitud positiva fue de 6.60 (4.98-8.77) y la razón de verosimilitud negativa de 0.08 (0.03-0.18).

La técnica de *Bootstrap* simple obtuvo 1,000 submuestras. Cuando se compararon los coeficientes de regresión obtenidos con el modelo final y los coeficientes de regresión obtenidos con las submuestras se observó que eran similares.

Los coeficientes de regresión del modelo final se encontraron dentro de los intervalos de confianza del 95% del *Bootstrap*, probándose así la validez interna del método.

En la muestra de validación externa se obtuvo un nuevo área bajo la curva COR de 0.93 (0.89-0.98), que no difirió estadísticamente de la obtenida con la muestra original, indicando que la prueba mantiene un buen poder de discriminación. Asimismo, en la muestra de validación la prueba Hosmer-Lemeshow mostró también una excelente calibración de la escala predictiva. Finalmente, la escala predictiva *TRAINS* reveló una eficacia en la muestra de validación similar a la obtenida en la muestra original con valores de sensibilidad del 92.31% (86.1%-100%) y especificidad del 85.1% (80.02%-90.18%). El índice de Youden para una puntuación ≥4 puntos fue de 0.77 (0.69-0.86), mientras que la razón de verosimilitud positiva fue de 6.19 (4.43-8.65) y la razón de verosimilitud negativa de 0.09 (0.04-0.23).

- **Conclusiones**

El análisis de la epidemiología de las lesiones traumáticas de aorta en Galicia mostró que la proporción de lesiones traumáticas de aorta entre los pacientes con traumatismo torácico cerrado mayor en nuestro hospital y en Galicia entre los años 2006 y 2010 fue del 4.4% y del 2.5%, respectivamente. De forma similar, la proporción anual de lesiones traumáticas de aorta entre los pacientes con traumatismo torácico cerrado mayor osciló en dichos años entre el 1.1% y el 3.3% anual en Galicia, mientras que en nuestra institución dicha proporción se situó entre el 2.5% y el 7.8% anual. Tras realizar un cálculo estimativo del número de pacientes con traumatismo torácico cerrado mayor y lesión traumática de aorta que fallecen en el lugar de accidente o durante su trasporte a un centro sanitario utilizando las referencias de las que disponemos en la literatura actual, se pudo inferir que la incidencia real de lesión traumática de aorta en Galicia se halla entre 3 y 6.1 casos por 100,000 habitantes y año.

Nuestra investigación confirmó que los pacientes con traumatismo torácico cerrado mayor presentan diferente perfil epidemiológico, pronóstico, presentación clínica inicial y número y distribución de lesiones no aórticas asociadas con respecto a los pacientes con traumatismo torácico cerrado mayor sin lesión aórtica en Galicia. Mientras la edad de los pacientes con traumatismo torácico cerrado mayor sin lesión aórtica presenta una distribución homogénea, la edad de los pacientes con lesión aórtica asociada se concentra entre los 16 y 35 años, hallándose el 54.6% de los pacientes con lesión aórtica en dicha franja de edad. Por otra parte, aunque hemos confirmado que el accidente de tráfico es la causa más frecuente de lesión traumática de aorta en traumatismo torácico cerrado en Galicia, hemos encontrado una proporción mayor de accidentes de motocicleta, precipitaciones y aplastamientos, así como una menor proporción de atropellos, como causa de la lesión aórtica con respecto a las cifras publicadas por otros autores.

En nuestro área comunitaria, hemos hallado que la proporción de lesiones aórticas “atípicas o no istmícas” (43.2%) es significativamente mayor que el 7% a 15% reportados en otras series clínicas, destacando también una proporción inusualmente mayor de lesiones traumáticas de arco aórtico (25%). Los pacientes con traumatismo torácico cerrado mayor y lesión aórtica han presentado inestabilidad hemodinámica en el momento de la admisión hospitalaria más frecuentemente que los pacientes con traumatismo torácico cerrado mayor sin lesión aórtica, así como una mayor proporción de lesiones extra-torácicas asociadas, lo que explica el peor pronóstico de este subgrupo crítico de pacientes con traumatismo torácico cerrado mayor.

En la segunda parte de la investigación se desarrolló un modelo predictivo multivariable para la lesión traumática de aorta en el contexto del traumatismo torácico cerrado mayor, que asocia una sensibilidad superior al 93% y una especificidad mayor al 85%. El pequeño número de pacientes con lesión traumática de aorta que fueron diagnosticados como falsos negativos (1.8%) presentaban lesiones aórticas de bajo grado. Por otra parte, la escala predictiva *TRAINS* demostró también su capacidad para diagnosticar lesiones traumáticas de aorta en traumatismos torácicos cerrados mayores en una muestra externa actual multicéntrica con una sensibilidad mayor del 92% y una especificidad superior al 85%, confirmando así su aplicabilidad en el momento actual y en diferentes regiones geográficas.

Asimismo, se demostró que las escalas generales de severidad convencionales para traumatismos no presentan una relación estadísticamente significativa entre la severidad del traumatismo y la severidad de la lesión traumática aórtica. En consecuencia, las escalas de severidad convencionales para traumatismos no son útiles para orientar un diagnóstico de sospecha de lesión traumática aórtica. Por el contrario, la puntuación obtenida en la escala *TRAINS* está relacionada con la severidad de la lesión aórtica, incluso en las lesiones aórticas de bajo grado.

En conclusión, la escala *TRAINS* y el algoritmo de manejo asociado han sido diseñados para su uso en la práctica clínica diaria con el fin de identificar de forma rápida y fácil los pacientes con traumatismo torácico cerrado mayor en riesgo de presentar una lesión aórtica asociada, lo que permite reducir la exposición a radiación ionizante y eliminar costes innecesarios en aquellos pacientes de bajo riesgo. Por otra parte, la escala *TRAINS* permite orientar un diagnóstico de sospecha incluso en pacientes con lesiones aórticas de bajo grado, los cuales requieren un seguimiento radiológico estricto para determinar su evolución y si requieren o no algún procedimiento adicional. El algoritmo *TRAINS* es además útil en la planificación del empleo de recursos en las unidades de trauma, permitiendo a los clínicos de hospitales primarios y secundarios derivar a los pacientes de alto riesgo de lesión aórtica a unidades especializadas, lo que aceleraría el diagnóstico y el establecimiento de un manejo terapéutico específico de este subgrupo crítico de pacientes traumatizados y reduciría la aparición de complicaciones aórticas potencialmente letales.

1. INTRODUCTION

In 1557, Belgian anatomist Andreas Vesalius described the first known case of aortic disruption caused by trauma. He discovered this injury while performing an autopsy on a patient who had fallen from a horse [1]. Nonetheless, it was not until the beginning of the twentieth century when acute traumatic aortic injuries (ATAIs) became more relevant to the medical community. In the era of high-speed transportation, patterns of traumatic aortic injury changed, with aortic injury becoming frequently noted in victims of airplane crashes during World War I [2].

Kuhn et al. [3] published 75 autopsy reports with ATAIs between 1895 and 1925. The lesions in all of these cases were confirmed by post-mortem examination. Between 1936 and 1942, in a series of more than 7,000 autopsies, Strassman et al. [4] found only 51 cases with ATAIs secondary to vehicular collision. In the early fifties the first series of surgical repair of traumatic aortic pseudoaneurysms were published by Goyette et al. [5], Jay et al. [6], Ware et al. [7], and Gerbode et al. [8], which drew more attention to this rising topic. However, it was not until 1958 when Loren Parmley, a pathologist in the US Army, described the clinical and pathological aspects of 296 patients with aortic disruptions caused by blunt trauma and defined the natural history of the injury [2]. This study, which still remains the largest pathological series to date, emphasized the relationship between the time of trauma and subsequent death, underlining the high lethality of untreated lesions.

Notwithstanding, within the past decade, along with advancements in technology, significant changes in the diagnosis and management of ATAIs have occurred. The widespread use of computed tomography for the diagnosis of ATAIs [9-11], clinical management with aggressive blood pressure control for patients who reach the hospital alive [12-14], the shift towards a more frequent use of endovascular techniques to repair this type of injuries [15], and the institution of surgical treatment in a delayed fashion after the stabilization of associated critical injuries [16] have changed the way ATAIs are managed.

The advent of new technologies for the diagnosis and treatment of ATAIs along with the availability at our institution of multidetector computed tomography (MDCT) for emergent patients since 2006, and the incorporation of emergent aortic endografting since 2003, prompted our team to review our early and long-term outcomes in managing major blunt trauma patients with ATAIs. This line of investigation resulted in several international publications about the non-operative treatment of ATAIs and about the special management of specific types of ATAIs that require special considerations. During the course of our research, we discovered that ATAIs, which are among the most lethal types of cardiovascular catastrophes, are rarely suspected in the initial evaluation of major trauma patients, and that the optimization of diagnostic resources and specific types of management were mandatory in these patients. Thus, we realized that an improvement in our clinical results depended on an earlier diagnosis and medical stabilization of major traumas with potential ATAIs and, eventually, the development of new strategies and algorithms for managing this critical subset of trauma patients. Hence, we devised this project in order to develop a simple and fast predictive score for ATAIs in major trauma patients and an associated algorithm that would potentially enable optimization of the use of clinical and diagnostic resources to provide and early and accurate diagnoses of patients at high risk of ATAIs. Furthermore, the use of such strategies would eventually reduce admission costs and nephrotoxic contrast and radiation exposure in low-risk trauma patients.

2. STATE OF THE ART IN ACUTE TRAUMATIC AORTIC INJURIES

2.1. Epidemiology

Nowadays, motor vehicle collisions (MVC) account for the majority of all cases of blunt trauma resulting in substantial injury to the thorax, followed by motorcycle crashes (MCC), falls from a height, auto vs. pedestrian (AVP), and crush injuries. The proportion of ATAIs among blunt trauma patients has increased along with the number of high-speed vehicle crashes.

Blunt aortic injury is the second most common cause of death following blunt trauma. Smith et al. [17] reported 387 cases of blunt trauma death and found that aortic injury was second only to head injury as the cause of death. More recently, in a multicentre study that enrolled 26,030 blunt trauma patients, Clancy et al. [18] identified 59 ATAIs that accounted for less than 1% of the admissions but were the second leading cause of death in blunt trauma.

From 1936 through to 1942, Strassman documented only 51 (0.73%) cases of ATAI resulting from motor vehicle crashes from among 7,000 autopsied victims [4]. As we have previously mentioned, in 1958, Parmley et al. [2] described an autopsy series of 296 victims of ATAI, which still remains the largest pathological series to date. Parmley et al. found that the highest rate of mortality occurred immediately after these injuries happened, that approximately 15% of aortas ruptured 6 hours after injury, and that approximately 25% ruptured 24 hours after the injuries were sustained [2].

Two decades later, studies by Greendyke et al. [19] and Sutorius et al. [20] found ATAI following fatal crashes in 10-15% of the victims. More recently, Dosios et al. [21] published a review of 1,980 autopsies of injury-related deaths and found 251 ATAIs (217 blunt and 34 penetrating traumas). Among the 217 ATAIs from blunt trauma, 62.9% occurred in traffic accidents (car and motorcycle crashes). Teixeira et al. [22] conducted a review of 304 full autopsies of blunt trauma fatalities and reported 102 (34%) ATAIs. The most frequent mechanism of blunt trauma with an associated ATAI was MVC (53/102; 52%), followed by AVP (38/102; 37.3%), MCC (7/102; 6.9%), and falls (3/102; 2.9%). Furthermore, the incidence of ATAIs among overall MVC fatal victims was 35.1% (53/151).

Despite improvements in the pre-hospital care system, a significant proportion of patients with ATAI do not reach the hospital alive and die at the scene or during transportation to the trauma centre [2, 21-24]. In clinical series, the majority of ATAIs also results from a sudden deceleration in MVCs. In both prospective multicentre studies of ATAIs conducted by the *American Association for the Surgery of Trauma*, $AAST_1$ and $AAST_2$ [15, 25], MVCs were responsible for 81% of the 274 and 67.7% of the 193 ATAIs reported, respectively. More recently, Arthurs et al. [26] conducted a study using the *US National Trauma Data Bank* from 2000 to 2005. During the study period, 3,114 patients with ATAIs were identified among 1.1 million trauma admissions (0.3%): 113 (4%) were dead on arrival, and 599 (19%) died during triage [26].

In addition to morbidity and mortality, another important variable related to the societal cost of injury is years of productive life lost (YPLL). This parameter reflects the potential productivity lost due to premature death. Trauma-related deaths result in a greater YPLL compared to cancer and cardiovascular deaths. For each traumatic death there are, on average, 36 YPLL, compared with 16 for cancer and 12 for cardiovascular diseases [27]. In the aforementioned study by Arthurs et al. [26], it was found that ATAIs resulted in poor function in those who survived to discharge. In fact, the investigators found that ATAI patients were less likely to be fully independent in terms of feeding (72% vs. 82%, $P < 0.05$), locomotion (33% vs. 55%, $P < 0.05$), and personal expression (80% vs. 88%, $P < 0.05$) compared to trauma patients without aortic injuries [26].

The most recent data provided by the *Community Road Accident Database* (CARE) of the European Commission (data available at http://ec.europa.eu/transport/home/care/index_en.html) revealed that there were more than 34,600 fatal victims in traffic accidents in the European Union in 2009. The 8% occurred in Spain. In order to perform international comparisons, it is generally accepted that a fatality from a traffic accident, also termed road death, is that occurring as a result of the accident from the time of the collision up to 30 days after it.

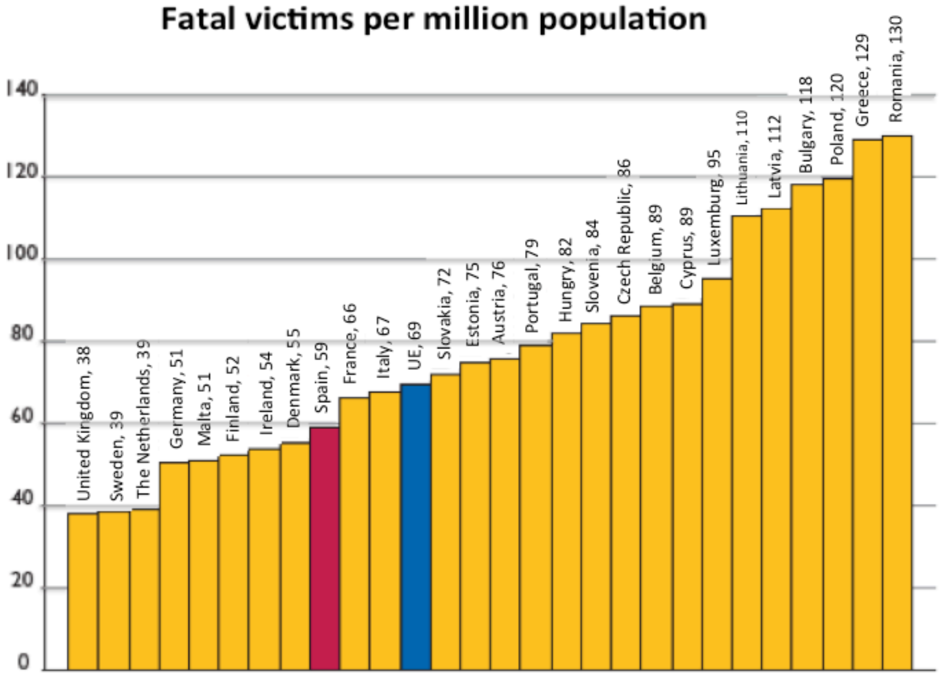
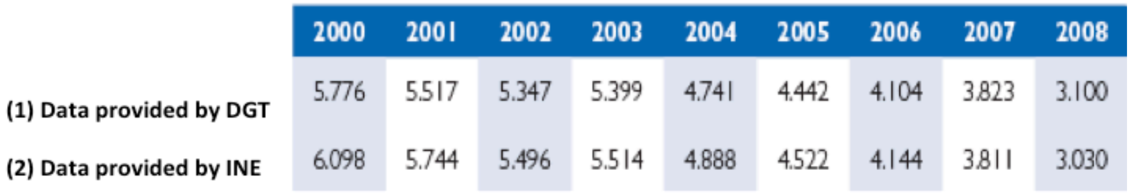


Figure 1. Distribution of fatal casualties per million population in the European Union in 2009 (*).

(*) Data provided by the *Community Road Accident Database* (CARE) and *Eurostat* (Statistical Office of the European Communities).

Although there has been a decreasing trend in the number of motor-vehicles accidents during the last decade in Spain, traffic accidents still remain as the first cause of death in population between 15-34 years olds. During the year 2009, there were 88,251 traffic accidents in Spain with victims, meaning that at least one person died or was injured in each of these. In these accidents, the total number of fatal victims due to motor-vehicle accidents (including cars, trucks, motorbikes and bicycles) was 2,714, considering also 470 people killed in pedestrian-vehicle accidents. The total number of injured casualties was 124,966, among which there were 13,923 severely injured casualties, defined as those who required more than 24 hours of hospital admission. At the end of the year 2009, the overall population in Spain was 47,021,031 million people (data provided by the *Instituto Nacional de Estadística* up to 01/01/2010, *Real Decreto 1612/2010*).



	2000	2001	2002	2003	2004	2005	2006	2007	2008
(1) Data provided by DGT	5.776	5.517	5.347	5.399	4.741	4.442	4.104	3.823	3.100
(2) Data provided by INE	6.098	5.744	5.496	5.514	4.888	4.522	4.144	3.811	3.030

Table 1. Evolution of the total number of road deaths (motor-vehicle and pedestrian-vehicle victims) in Spain from 2000 to 2008.

(1) Database provided by *Dirección General de Tráfico (DGT).* Data obtained by law agents. A fatality from a traffic accident is considered as a death up to 30 days after the accident (www.dgt.es/portal/es/seguridad_vial/estadistica/publicaciones/princip_cifras_siniestral.do).

(2) Database provided by *Instituto Nacional de Estadística (INE)* considering deaths according to the cause of death. There is no time limit between the traffic accident and death (www.ine.es).

In 2009, road deaths were more common in victims between 25 and 34 years old, with a total number of 572 motor-vehicle accident casualties, followed by 490 victims between 35 and 44 years old.

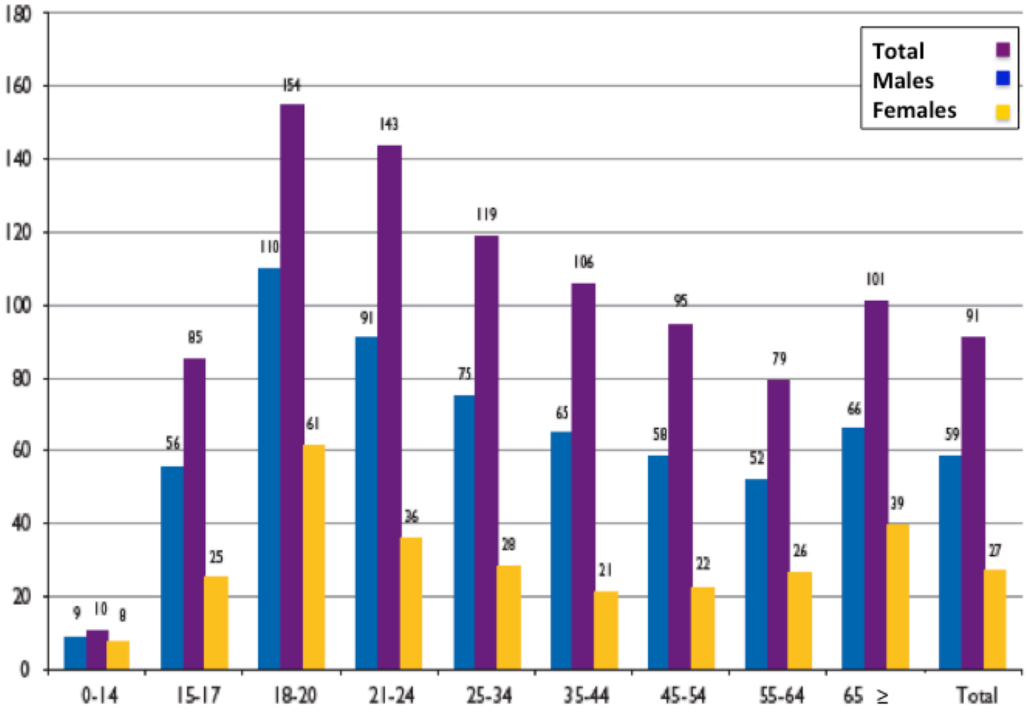


Figure 2. Distribution of fatal casualties by age and sex per million population in Spain in 2009.

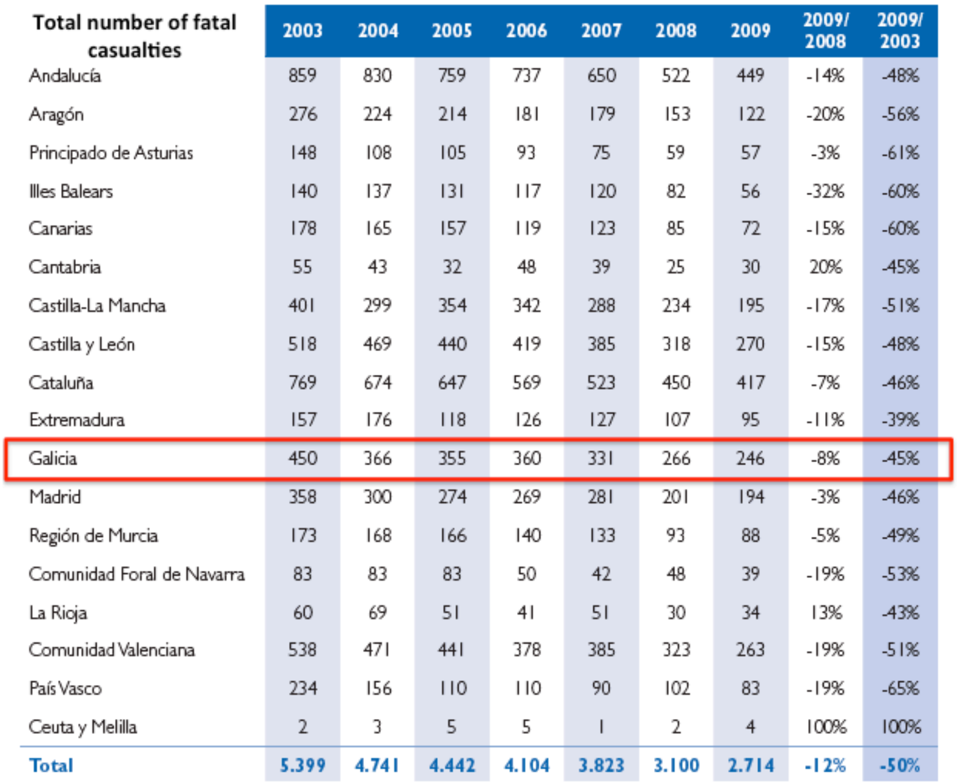
The higher rate of road deaths per million population occurred in the group of victims aged 15 to 24 years old in 2009.

In 2009, 470 pedestrians died in motor vehicle-pedestrian accidents, comprising 17.3% of the total road deaths registered in Spain that year.

Year	Dead pedestrians	Percentage of dead pedestrians over overall road deaths
2000	898	15.5%
2001	846	15.3%
2002	776	14.5%
2003	787	14.6%
2004	683	14.4%
2005	680	15.3%
2006	613	14.9%
2007	591	15.5%
2008	502	16.2%
2009	470	17.3%

Table 2. Number of pedestrians who died in pedestrian-vehicle collisions and number of pedestrians killed as a percentage of the overall road deaths in Spain.

Regarding the different Spanish regions, the total number of fatal casualties in motor-vehicle accidents decreased. As we can see in Table 3, the total number of road deaths in Galicia in 2009 was 246 victims in motor-vehicle and pedestrian-vehicle accidents. Our region, Galicia, experienced a decrease of 45% in the total number of road deaths compared to the numbers in 2003 and 2009. At the end of the year 2009, the overall population in Galicia was 2,797,653 million people (data provided by the *Instituto Nacional de Estadística* up to 01/01/2010 *Real Decreto 1612/2010*).



Total number of fatal casualties	2003	2004	2005	2006	2007	2008	2009	2009/ 2008	2009/ 2003
Andalucía	859	830	759	737	650	522	449	-14%	-48%
Aragón	276	224	214	181	179	153	122	-20%	-56%
Principado de Asturias	148	108	105	93	75	59	57	-3%	-61%
Illes Balears	140	137	131	117	120	82	56	-32%	-60%
Canarias	178	165	157	119	123	85	72	-15%	-60%
Cantabria	55	43	32	48	39	25	30	20%	-45%
Castilla-La Mancha	401	299	354	342	288	234	195	-17%	-51%
Castilla y León	518	469	440	419	385	318	270	-15%	-48%
Cataluña	769	674	647	569	523	450	417	-7%	-46%
Extremadura	157	176	118	126	127	107	95	-11%	-39%
Galicia	450	366	355	360	331	266	246	-8%	-45%
Madrid	358	300	274	269	281	201	194	-3%	-46%
Región de Murcia	173	168	166	140	133	93	88	-5%	-49%
Comunidad Foral de Navarra	83	83	83	50	42	48	39	-19%	-53%
La Rioja	60	69	51	41	51	30	34	13%	-43%
Comunidad Valenciana	538	471	441	378	385	323	263	-19%	-51%
País Vasco	234	156	110	110	90	102	83	-19%	-65%
Ceuta y Melilla	2	3	5	5	1	2	4	100%	100%
Total	**5.399**	**4.741**	**4.442**	**4.104**	**3.823**	**3.100**	**2.714**	**-12%**	**-50%**

Table 3. Distribution of road deaths by Spanish regions between 2000 and 2009.

Unfortunately, exact data about the total number of ATAIs diagnosed and/or treated yearly in Spain are not available, neither from clinical series nor autopsy series. Also, no information is available regarding in-hospital admissions and/or mortality due to falls or occupational accidents in Spain. Therefore, we used the data on ATAI incidence reported in clinical and autopsy series from other countries. Thus, according to the data given and assuming a proportion of 20-30% of ATAIs among road deaths, up to 900 of the 3,100 fatal victims in 2009 in Spain may have sustained an ATAI, and may potentially have benefited from an early diagnosis of the aortic injury. On the other hand, we should also consider the fact that among these potential 900 fatal victims the death rate at the scene of the accident, as reported in the literature, ranged from 45% [24] to 83% [21, 22], and that the death rate during transportation was around 11.5-12% [21, 24]. In contrast, the 13,923 severely injured patients admitted to hospitals during the same year are clearly our target population because these trauma patients should have undergone an easy and low-cost screening test for ATAIs; thus, patients at high risk of suffering an ATAI would potentially have benefited from an early diagnosis of aortic injury, while avoiding unnecessary costs among those patients at a low-risk of ATAI trauma.

BRIEF SUMMARY

Motor vehicle accidents account for the majority of all cases of ATAIs, followed by falls from a height, auto vs. pedestrian and crush injuries. Blunt aortic injury is the second most common cause of death following blunt trauma. The highest rate of mortality occurs immediately after the trauma and can reach 25% in the first 24 hours after the aortic injury is sustained. In addition to morbidity and mortality, ATAIs entail an important societal cost in years of productive life lost and poor functional outcomes and dependence of the patients.

2.2. Natural history and prognosis of ATAIs.

The natural history of an ATAI in a given patient is dependent on many factors, where an early diagnosis is of paramount importance. Nowadays, survival rates are based on data drawn from autopsy series and operative series.

The classic series reported by Parmley et al. in 1958 documented a death rate at the scene of as high as 85% and a subsequent mortality rate in non-operated survivors of 1% per hour for the first 48 hours [2]. Most of these aortic injuries represented full-thickness tears that resulted in rapid exsanguination before definitive therapeutic intervention [2]. Furthermore, the early work of Parmley et al. [2] suggested that of the patients who survived long enough to reach medical care, death would have occurred within 48 hours for 39% and within 4 months for 89% [2]. Nonetheless, a minority of aortic injuries are incomplete or contained, and 13-23% of patients may survive to presentation at the trauma centre [17]. If left untreated, such injuries may progress to complete rupture or they may lead to a pseudoaneurysm with the potential for late rupture. It has since been discovered that the rate of acute mortality can be 40% to 70% and that patients admitted with ATAI fall into two broad categories [28, 29]. A small number, approximately 5%, are haemodynamically unstable or deteriorate within 6 hours of admission. All-cause mortality in this group invariably exceeds 90%. The remainder are haemodynamically stable and afford time for workup and the staging of any intervention. Mortalities in this latter group, for which the rate is as low as 25%, are rarely from free rupture if blood pressure is controlled; they are more commonly from a consequence of associated injuries. Recently published autopsy series reported a death rate at the scene of the accident from 45% [24] to 83% [21, 22], and a death rate during transportation of around 11.5-12% [21, 24]. In fact, in a series of 242 autopsies, Burkhart et al. [24] reported that 3% of patients died during the first 30 minutes after hospital admission; 34% between 30 minutes and 4 hours; 4% between 4 and 8 hours, and less than 2% of the patients survived more than 8 hours after hospital admission. Karmy-Jones et al. [30] noted that there were three broad categories of patients who sustained an ATAI. The largest group (70% to 80%) comprised those who died at the scene. Victims of the second category were unstable when they presented to the hospital or became unstable shortly after, and only represented 2% to 5% of patients with an ATAI. The final group (20% to 25%) remained haemodynamically stable from the aortic injury, and any mortality was secondary to associated injuries.

Another factor to consider is that autopsy studies tend to overestimate the mortality rates, while operative studies tend to underestimate it. In the most recent surgical series mortality rates ranged from 0 to 50% and varied depending on the size of the series, although the rates of attributable-mortality were not clearly defined [15, 26, 31-35]. In a previously cited review of 3,114 ATAIs identified among more than 1.1 million trauma patients from the *US National Trauma Data Bank*, Arthurs et al. [26] evaluated initial physiological variables, associated injuries, and the type of aortic repair as potential factors associated with deaths in patients with ATAI. Factors that predicted a worse outcome included: increasing age, hypotension on admission, hypothermia upon admission, major head injury (Abbreviated Injury Score (AIS) >3), major abdominal injury (AIS >3) and Injury Severity Score (ISS) >25. Other variables such as admission GCS, base deficit, delayed aortic repair (>72 hours), laparotomy, major pelvic injury and year of admission did not significantly influence the outcome [26].

Variable	**Adjusted odds ratio**	**95% confidence interval**	***p*-value**
Age (per year)	1.04	1.03-1.05	<0.05
Hypotension (SBP <90 mmHg) and hypothermia (T <35 ºC)	5.02	3.65-7.34	<0.05
Major head injury (AIS ≥3)	1.50	1.00-2.23	<0.05
Major abdominal injury (AIS ≥3)	1.77	1.19-2.65	<0.05
Injury severity score >25	2.17	1.28-3.66	<0.05
Aortic repair	0.36	0.24-0.54	<0.05

Table 4. Logistic regression analysis of physiological factors, associated injury patterns and aortic repair as potential factors associated with mortality in patients with ATAI from Arthurs et al. [26]. (AIS=abbreviated injury score; SBP=systolic blood pressure).

The authors found that aortic repair was the only variable associated with improved survival (OR = 0.36; 95% CI: 0.24-0.54, $P < 0.05$) when controlling for physiological presentation and associated injuries [26].

We recently published the largest series with the longest follow-up of non-operatively managed ATAIs to date and reported a long-term survival of non-operative managed ATAI patients of 75.6% at 1 year, 72.3% at 5 years and 66.7% at 10 years [36].

BRIEF SUMMARY

Major blunt trauma patients with ATAIs can be classified into three broad categories. The largest group (70% to 80%) comprises those who died at the scene. Most of those aortic injuries represent full-thickness tears that result in rapid exsanguination. The second category includes the 2%-5% of patients with an ATAI who are unstable when they reach the hospital or become unstable shortly after. The overall mortality rate in this second group exceeds 90%. The final group, involving 20% to 25% of patients, remains haemodynamically stable from the ATAI and present an overall in-hospital mortality rate of around 25%, mainly secondary to associated injuries.

2.3. Mechanisms of injury

There is considerable uncertainty regarding the actual mechanism of injury in aortic blunt trauma. The process is likely the result of both anatomical and mechanical factors. The majority of ATAIs result from violent deceleration, most commonly as a result of an MVC, especially head-on and side-impact collisions. Some of the earliest investigators proposed that ATAIs had a relatively simple univariate aetiology, such as a sudden and dramatic rise in arterial blood pressure [37, 38], while more contemporary theories propose that ATAIs are the result of a complex multivariate process secondary to a combination of stresses [39, 40]

The mechanisms currently being proposed as contributing to ATAIs include shearing forces, rapid deceleration, hydrostatic forces and the osseous pinch [41-43].

2.3.1. Stretching and shearing forces

The first investigator to propose a fundamental mechanism for ATAI was possibly Rindfleisch [44], who suggested that this injury was caused by a sudden stretching of the aorta. Other investigators also attributed rupture to a stretching response [45]. The rationale for this was the common belief that the aorta is inherently weaker at the isthmus, as established through a series of tensile tests conducted on aortic samples by Lundewall [46]. Furthermore, several investigators emphasized the importance of the descending aorta fixed to the spine by the mediastinal pleura relative to the more mobile arch and ascending aorta as an important contributory factor [45, 47, 48].

Parmley et al. [2] pointed out the fact that the most common cause of traumatic aortic injuries is the force generated by rapid deceleration of the body in either the vertical or horizontal plane. Indeed, deceleration sets up differential forces between the various organs and tissues of the body depending on their structure, location and attachments, and the direction of deceleration [2]. Rapid deceleration in the anteroposterior and lateral directions has been shown to be sufficient to result in cardiac displacement, producing torsion and shearing forces against the aorta at levels of relative immobility, mainly the ligamentum arteriosum, aortic root, and diaphragm [24]. The "whiplash" mechanism that occurs in anteroposterior deceleration thoracic trauma was first described by Zehnder et al. [49]. With abrupt deceleration of the thorax, such as that which occurs in high-speed vehicular accidents where the body is violently thrown against a stationary object, the ligamentum arteriosum, supra-aortic vessels and intercostal arteries anchor the middle arch and mid-distal descending aorta to the thorax. These portions decelerate with the thorax, whereas the distal end of the aortic arch and the upper descending thoracic aorta continue to move forward and decelerate later. Thus, ATAIs tend to occur at the interface between parts with different mobility. Nevertheless, anteroposterior deceleration is only responsible for the aortic stretching and the resulting shear forces. Lateral compression can also result in severe internal chest deformation and shearing forces at the aortic isthmus [50, 51].

Katyal et al. [50] conducted a study to determine the relationship between ATAIs and the direction of impact at the time of a motor vehicle crash in a series of 97 patients, and concluded that in 49.5% of the cases the ATAI was the result of a lateral impact crash. In this series, 94% of the ATAIs occurred at the peri-isthmic region [50].

The sum of the tensile vectors is complex. The results of tensile tests conducted on samples of aorta have shown that it is capable of sustaining strains of up to 80% of its original dimension prior to rupture [52, 53]. Consequently, if the isthmus section of the aorta ruptures under tension, it is rationalised that the stretching of the aorta must be very localised in order for it to be stretched to the required strain of rupture within the confines of the thoracic cage.

A direct force that results in fracture or displacement of one of the dorsolumbar vertebrae may also cause rupture of the aorta by shearing action.

In addition, the deceleration mechanism of aortic injury after blunt thoracic trauma has never adequately explained other unusual sites of aortic wall injury [54].

2.3.2. Intravascular pressure

In the first half of the twentieth century, ATAI was also attributed to a sudden rise in blood pressure [37, 38, 55]. However, more recent studies have cast doubt on this hypothesis, rationalizing that if the aorta were an isotropic cylindrical vessel under pressure it would rupture longitudinally rather than transversely. The typically observed transverse tears in the aorta could only occur if the transverse strength was more than twice the longitudinal strength. Tensile tests performed by Mohan et al. [52, 53] showed that the ultimate tensile strength of the aorta in the transverse direction relative to the longitudinal direction nearly approximates the required rupture ratio of 2:1. Mohan et al. [52, 53] demonstrated this point in bi-axial inflation tests conducted on aortic tissue samples. In these tests, the aorta samples consistently failed transversely.

Some investigators conducted studies to establish the burst pressure of the aorta. Oppenheim et al. [37] stated that the aorta bursts under a pressure of around 4.0×10^5 N m^{-2}, whereas Klotz et al. [38] found that inflating the aorta up to a pressure of 4.0×10^5 N m^{-2} did not produce a single rupture. However, the results by Klotz et al. may have been jeopardized because their analyses were conducted on aortic samples at post-mortem, so the vessels may have suffered a change in their mechanical properties that was significant enough to influence their results.

As part of the *Crash Injury Research Engineering Network* (CIREN), Siegel et al. [56] developed a computer simulation and validation of the Archimedes Lever hypothesis as a mechanism for aortic isthmus injury in lateral MVCs. According to this hypothesis, the intrathoracic aorta would suffer a great increase in intravascular pressure following a lateral impact causing it to behave as a rigid lever system. The long arm of the lever would be the proximal aorta and the short arm the isthmus, fixed distally at the descending aorta. The left subclavian artery would act as the fulcrum so impact forces would be magnified at the isthmus by an Archimedes effect.

2.3.3. Water-hammer effect

Zehnder [49, 57-59] calculated that an intravascular pressure of around 2,500 mmHg would be required to rupture the aorta. Increased intravascular pressure can exceed 2,000 mmHg following direct compression of the aorta, and this was termed the "water-hammer effect" [60]. Lundewall [46] was the first author to suggest that ATAI was the result of a "water-hammer effect".

A "water-hammer effect" results when the flow of a non-compressible fluid is dramatically occluded, which leads to high-pressure waves being reflected back along the vessel wall. During a vehicle impact it is thought that the aorta may be occluded at the point where it passes through the diaphragm as a result of the abdomen being compressed. The pressures created by this mechanism have been shown to result in mainly transverse tears at the level of the isthmus [46], but it can also cause retrograde injury at the aortic root [43]. Kivity et al. studied the action of this hydrostatic response of the aorta [61]. These investigations found that a sudden occlusion of blood flow in the aorta would lead to a significant pulse of pressure in the aorta. This would be expected to be significantly greater at the aortic arch on account of the curvature reflecting and intensifying the pressure wave. However, these analytical studies were unable to take into account the additional deformation of the aorta during an impact where increasing the curvature of the aorta could possibly lead to greater increases in the pressure wave in this region. More recently, Pearson et al. [62] performed a series of experimental tests and concluded that a pressure spike alone is unlikely to be the primary cause of aortic injury, but it may well be a prerequisite for such an injury.

2.3.4. Osseous pinch

Penetrating injuries from rib and thoracic vertebral body fractures can also cause a direct injury of the thoracic aorta [63, 64]. The mechanism called the "osseous pinch" results from direct compression of the aorta between the anterior chest wall and the thoracic spine [41, 42]. An animal model study by Crass et al. [41] showed that anteroposterior compression of the chest consistently results in transverse lacerations to the aortic isthmus when compressed between the anterior bony structure and the thoracic spine. The compressive forces present in blunt thoracic trauma depress the anterior thoracic osseous structures, causing them to rotate posteriorly and inferiorly about the posterior rib articulations. However, the specific anterior bony structure that causes vascular injury may vary. This mechanism could also explain concomitant injuries at branch vessels [41, 42]. Cohen et al. reported calculations made from the cross-sectional anatomy shown on CT scans and provided the first in vivo support for the "osseous pinch" mechanism of traumatic aortic injury [42].

2.3.5. Multivariate complex models

More contemporary theories propose that ATAIs results from a combination of mechanisms including shear, torsion and stretching forces, compounded by hydrostatic forces [39, 62, 65].

An alternative mechanism in MVC, called the "shovelling effect", involves the compression force of the steering wheel on the sternum and abdomen, causing the mediastinum to displace upwards. As the chest is compressed, the heart is squeezed between the sternum and the spine forcing blood from the heart into the aorta and increasing the blood pressure of the aorta and pulmonary trunk. Moreover, at the level where the aorta passes through the diaphragm, the aorta may be kinked, occluding the blood flow and contributing to the rise in aortic blood pressure. This sudden occlusion of the blood flow can lead to high pressure waves in the aorta due to the aforementioned "water-hammer" effect.

The "shovelling effect" displaces the heart and aortic arch upwards while the descending aorta, which is tethered to the spine via the lungs, remains fixed. The isthmus region of the descending aorta, which is at the junction between the fixed descending and upwards displaced aortic arch, is placed under a torsional and tensile load; being inherently weaker than the rest of the vessel, the aorta then tears at the isthmus.

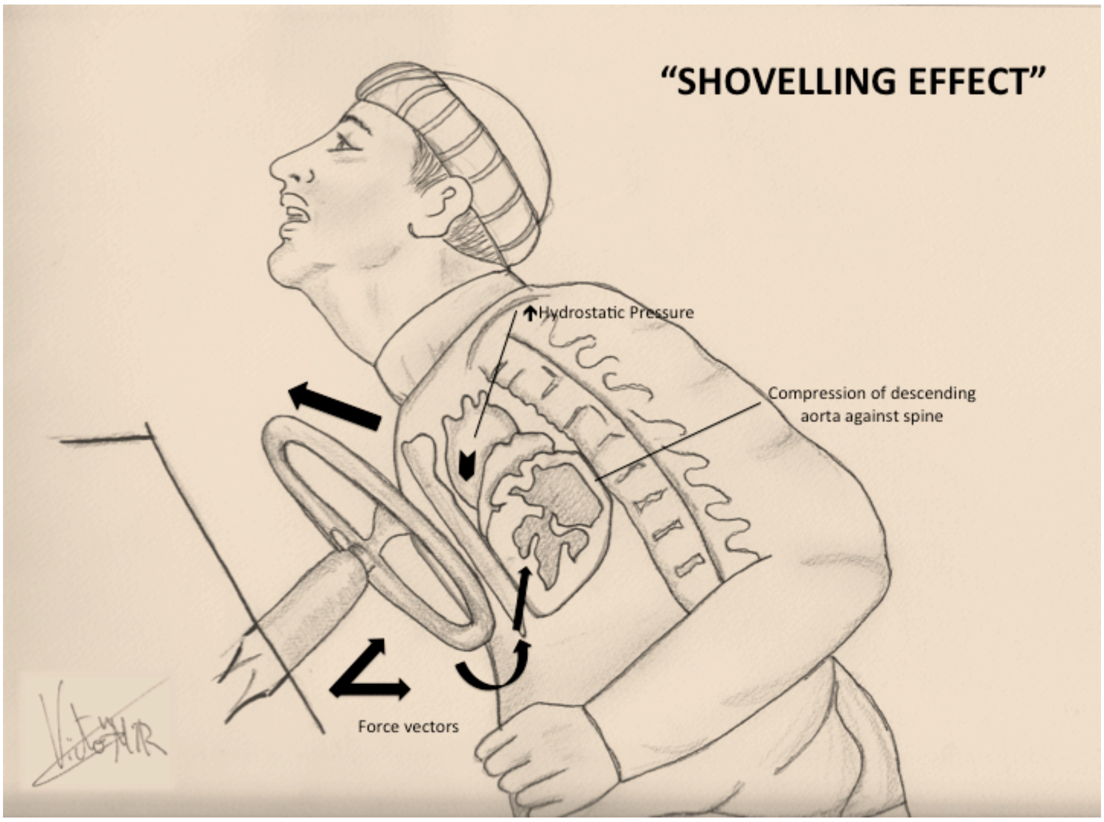


Figure 3. The "Shovelling effect". The "shovelling effect" has been proposed as being one of the more complex mechanisms of ATAIs in car accidents, in which the asymmetrical impact of the steering wheel on the chest displaces the heart and aortic arch upwards while the descending aorta remains fixed.

Gotzen et al. [66] proposed that the direction of the impact to the chest and the resulting deformation of the thorax significantly affect the type of mechanisms that contribute to aortic rupture. These authors analysed cases of aortic rupture and proposed that impact to the chest from the right ventro-caudal to the left dorso-caudal predominated. They surmised that this type of impact would force the heart and aortic arch upwards posteriorly and to the left, leading to stretching and shearing of the aorta at the isthmus. Gotzen et al. [66] also found that ATAI at the isthmus was not as common if the impact was directed from the left ventro-caudal to the right dorso-caudal.

Richens et al. [39] developed a finite element model of the aorta to investigate the mechanical initiators of ATAI. The authors suggested that susceptibility to ATAI may be dependent on the position within the cardiac cycle, the position within the pulmonary cycle, and the volume loading of the vasculature [39]. Likewise, Kivity et al. [61] surmised that ATAI is more likely to occur at the start of diastole when the aorta is full of blood and in its maximum state of pressurization. In addition, the state of the lungs could potentially provide additional cushioning or, conversely, a greater loading of the aorta during impact to the chest.

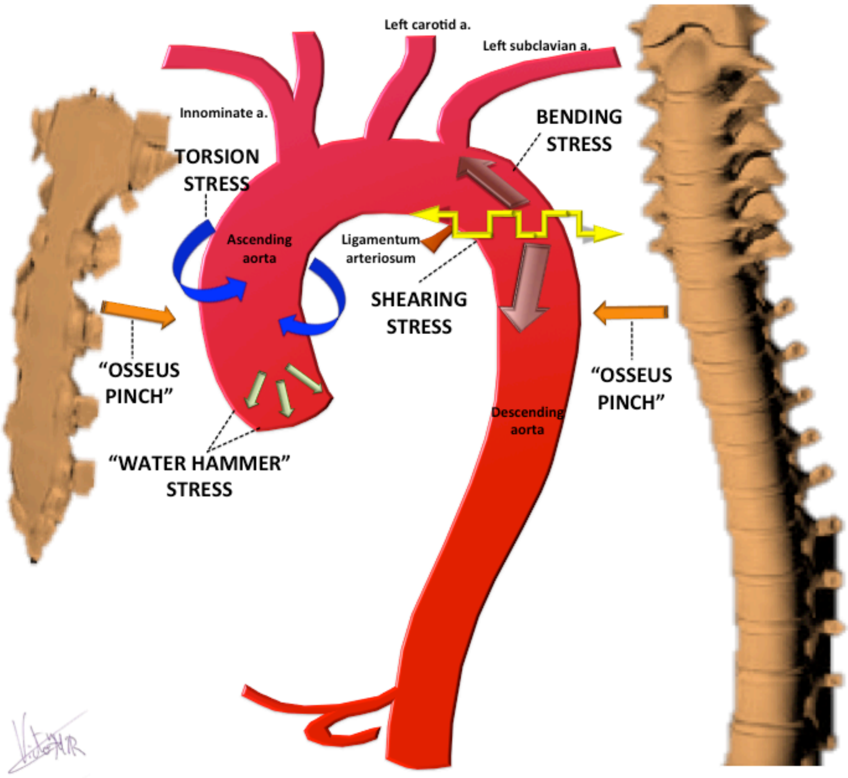


Figure 4. Mechanisms of injury resulting in ATAIs. The osseous pinch (orange arrows) is shown by posterior displacement of the sternum and by compression of the aorta against the thoracic spine. Torsion is depicted in the ascending aorta (curved blue

arrows), resulting in twisting above the fixed aortic valve. Compression of the lumen forces blood inferiorly towards the aortic valve, resulting in the "water hammer effect" (green arrows in the aortic root). At the ligamentum arteriosum, the aorta is affected by both bending (dark red arrows) and shearing (yellow arrow) stresses.

2.3.6. Additional factors in the pathogenesis of ATAI

It has been speculated that under a specific set of conditions certain groups of the population may be more susceptible to ATAI than others. The elastic lamina of the aorta can become frayed or destroyed in various diseases such as advanced atherosclerosis, connective tissue disorders or syphilitic aortitis, and such changes can render it more susceptible to traumatic laceration. The amount of the amorphous intercellular substance in the intima and media increases in atherosclerosis and accumulations of this material, often with focal pooling and vacuolization, characterize the lesions of idiopathic cystic medial necrosis of the aorta. Hence, it would appear that an abnormal accumulation of the amorphous intercellular substance must be considered when evaluating the effect of trauma on the aorta. These could contribute to the initiation of injury if present within an individual but, as discussed by Shkrum et al. [47], they are not a pre-condition for the occurrence of ATAI. A more common factor is the detrimental effect of age on the mechanical properties of the aorta through arteriosclerosis, reducing the ultimate tensile strength and strain of the vessel [52]. Again, although this could contribute to the onset of injury, there is no evidence to suggest that it is a pre-condition of injury as this injury has been shown to occur in significant numbers in all age ranges.

BRIEF SUMMARY

Contemporary theories propose that ATAI is a complex multivariate process secondary to a combination of stresses, including shearing forces, rapid deceleration, hydrostatic forces and the osseous pinch.

Rapid deceleration in the anteroposterior and lateral directions is the most common mechanism of aortic wall injury, producing torsion and shearing forces against the aorta at levels of relative immobility, mainly affecting the ligamentum arteriosum, aortic root and diaphragm. The direction of impact to the chest and the resulting deformation of the thorax significantly affect the type of mechanism that contributes to aortic rupture. Other influencing variables are the position within the cardiac cycle, the position within the pulmonary cycle, and the volume loading of the vasculature at the time of impact.

Finally, there is likely to be a specific set of conditions that potentially contribute to the onset of aortic injury, such as advanced age, arteriosclerosis or connective tissue disorders.

2.4. Pathology of ATAI

2.4.1. Morphology of ATAI

The various forms of ATAI, from limited lacerations of the intima to complete transection of the aorta, depend on the morphological structure of the arterial wall and the strength of the forces causing the trauma. Acute traumatic aortic injuries typically involve a transverse tear in the wall of the aorta, with all the three layers of the vessel wall being disrupted [2, 21-24]. The extent of the damage varies considerably between cases. In mild trauma, the injury may only be a partial circumferential tear in the intima that may extend into the medial layer of the aortic wall [45]. Partial disruptions and spiral injuries occur less frequently and are associated with intramural haematomas and focal dissections, unlike complete transections [2]. Partial tears are usually posterior and involve the vessel intima and media, leaving the adventitia intact. Under such circumstances the intact adventitia may be strong enough to contain the circulation within the aorta and the individual stands a chance of survival [48, 67]. In more severe cases the tear can also extend into the adventitial layer, leading to a partial or complete transection of the aorta. Initial survivors usually have an incomplete transection, with disruption of the media and intima only, although some patients have survived circumferential, full-thickness disruptions. Following a complete transection, blood exanguinates into the mediastinum and pleural cavity and the victim usually dies [2]. Nonetheless, there are reports in the published literature about patients suffering a complete transection of the aorta but managing to survive for an adequate period to allow medical intervention [2, 68].

Arterial blood pressure can force blood between the layers of the aortic wall, forming a pseudoaneurysm. In the case of chronic pseudoaneurysms, blood flows into the false aneurysm, which later thromboses and forms a fibrous wall that then tends to calcify [69-71]. Post-traumatic aneurysms have been known to fistulize to the pulmonary artery or bronchus [72-74] or cause dyspnoea compressing the left main bronchus [75].

2.4.2. Anatomic location of ATAI

In contrast to the anatomical extent of the aorta, ATAIs are limited to only a few specific locations along its length. Most injuries occur at the aortic isthmus, just distal to the left subclavian artery, followed by, in order of decreasing frequency, the ascending aorta, aortic arch, distal descending aorta and abdominal aorta. Clinical series have shown that injuries occur at the isthmus in 54.7% to 74.5% of cases, the ascending aorta in 1% to 3.6% of cases, the arch in 5.7% to 18% of cases, the distal descending aorta in 2% to 21.8% of cases, and simultaneously at multiple locations in 2% to 5% of cases [15, 25, 32, 76-78].

Non-isthmus or "atypical" aortic injuries are remarkably more frequent in autopsy studies than in clinical practice. Originally, Parmley et al. presented a series of 171 autopsies with ATAIs located at the isthmus in 55.6% of cases, the descending aorta in 15.8%, the ascending aorta in 9.9% and the abdominal aorta in 6.4% [2]. These authors also reported multiple aortic injuries in 2.9% of the victims [2]. A more recent autopsy series reported an incidence of traumatic aortic injuries at the isthmus in 44% to 66% of the victims, in the ascending aorta in 5% to 12.6%, in the arch in 2% to 11%, in the descending aorta in 0.9% to 12%, in the abdominal aorta in 0.9% to 6%, and simultaneously in multiple locations in 16% to 32% as shown in Table 5.

Author	**Year**	**No. victims**	**Ascending aorta (%)**	**Arch (%)**	**Isthmus (%)**	**Descending aorta (%)**	**Abdominal aorta (%)**	**Multiple sites (%)**
Parmley[2]	1958	275	64 (23.3%)	22 (8%)	124 (45.1%)	35 (12.7%)	13 (4.7%)	17 (6.2%)
Feczko[23]	1990	142	11 (8%)	3 (2%)	76 (54)%	17 (12%)	9 (6%)	26 (18%)
Dosios[21]†	2000	217 †	21.6%†	8.3%†	59.4%†	31.3%†	NS	NS
Burkhart [24]	2001	241	19 (8%)	7 (3%)	140 (58%)	24 (10%)	13 (5%)	29 (16%)
Prijon[79]	2009	230	29 (12.6%)	5 (2.2%)	102 (44.3%)	2 (0.9%)	2 (0.9%)	74 (32%)
Teixeira[22]	2011	102	5 (5%)	11 (11%)	67 (66%)	††	NS	18 (18%)

Table 5. Location of traumatic aortic injuries in the autopsy series. †The sum of percentages in each row may exceed 100 as a result of multiple aortic injuries being recorded in several victims. Absolute numbers are not specified in the study by Dosios et al. [21].

††Teixeira et al. [22] reported isthmus and descending aorta injuries altogether (NS: not specified).

Multiple aortic injuries appear to be more common in autopsy series than in clinical series [21-24]. Multiple intramural and/or transmural aortic injuries can occur up to 32% of cases, in which the dominant rupture is the leading rupture with several secondary concomitant ruptures at a distance of 5-25 mm [2, 22-24, 79].

After showing that injuries to the aortic isthmus were less frequent in autopsy studies than in clinical studies, several authors suggested that non-isthmus or “atypical” injuries of the aorta are more lethal [21-24]. The rationale behind this may be that a greater number of patients with injuries occurring at the isthmus survive longer, owing to the protective effect that may be provided by the mediastinal periadventitial tissues surrounding the isthmus. Besides this, both relevant clinical and autopsy series seem to concur with the very poor prognosis of traumatic ascending aorta and aortic arch injuries.

2.4.3. Classification of ATAI

A review of the literature revealed that different terms are used to describe particular forms of ATAI, which can lead to the misinterpretation of findings or diagnoses. Several classifications have been proposed based on imaging, surgical or autopsy findings.

Originally, Parmley et al. [2] classified traumatic aortic injuries according to the extent of the involvement of the aortic wall, as follows:

- **Type 1. Intimal haemorrhage.** Areas of intimal haemorrhage, occasionally described in association with fatal lesions.
- **Type 2. Intimal haemorrhage with lacerations.** This lesion differs in that the endothelial surface of the aorta is broken and the collagenous and elastic fibres of the subendothelial layer of the intima are more severely disrupted and separated by haemorrhaging.
- **Type 3. Medial lacerations.** These lacerations extending into, but not through, the tunica media. They can appear in association with other aortic lesions, but sometimes they are alone.
- **Type 4. Complete laceration of the aorta.** This is a complete rupture of the aorta, including the adventitia and the attached connective tissue.
- **Type 5. False aneurysm formation.** This includes all cases of aneurysmal bulging of the aortic wall followed complete laceration of the intima and media, and also cases where a false aneurysm formed after the rupture of all three layers. In cases where circumferential laceration of the intima and media was

complete, a fusiform aneurysm developed, whereas in cases where only a portion of the wall was lacerated a saccular aneurysm formed.

- **Type 6. Periaortic haemorrhage.** This injury often accompanies complete rupture or other traumatic lesions of the aorta, but it occasionally occurs independently.

In 1995, Vignon et al. [80] defined four distinct types of traumatic aortic injury, combining the anatomical classification of Parmley et al. [2] and their results from the review of the TEE findings in 32 consecutive major trauma patients with ATAI:

- **Traumatic aortic intimal tears**. In these lesions, the integrity of the aortic medial and adventitial layers is preserved (type 2 lesion in the classification of Parmley et al.[2]). Subadventitial traumatic aortic disruptions involve the entire aortic intimal and medial layers. In these lesions, the threat of adventitial rupture causing a massive haemorrhage is constantly present.
- **Partial aortic disruption**. These injuries appear as a limited discontinuity of both intimal and medial layers. They can be associated with or without pseudoaneurysm formation.
- **Subtotal aortic disruption**. These lesions involve more than two thirds of the circumference of the aortic wall. A narrow band of aortic wall, usually found in the posterior aspect of the aorta, secures the disrupted aortic segments a few centimetres apart.
- **Complete aortic disruption**. These lesions involve the entire circumference of the aorta. Usually, in both subtotal and complete subadventitial aortic disruptions, medial flaps are observed. The presence of a subadventitial

horizontal disruption is associated with a circular pattern of the medial flap, whereas the medial flap is linear in cases of subtotal lacerations.

More recently, Prijon et al. developed a morphological classification after reviewing 230 autopsies with 355 ATAIs [79]. This classification includes three basic types with corresponding subtypes:

- **Type I (intramural) ruptures:**
    - **IA**: rupture of the tunica intima.
    - **IB**: rupture of the tunica intima and the inner layer of the tunica media.
    - **IC**: rupture of the intima and media to the adventitia.
    - **ID**: post-traumatic false aneurysm or pseudoaneurysm.
- **Type II (transmural) ruptures:**
    - **IIA**: partial transmural rupture (small degree of transmural rupture).
    - **IIB**: total transmural rupture or transection (transmural rupture through the entire circumference of the aorta).
    - **IIC**: rupture of post-traumatic false aneurysm or pseudoaneurysm.
- **Type III (multiple) ruptures:**
    - **IIIA**: multiple type I ruptures.
    - **IIIB**: multiple type I and type II ruptures.
    - **IIIC**: multiple type II ruptures.

The classification proposed by Prijon et al. [79] is useful for precisely defining ATAIs in autopsy studies, but it presents several shortcomings for use on a daily clinical basis.

Another classification system for ATAIs was proposed by Azizzadeh et al. [33, 81] in 2009 using imaging data. This classification is based on injury severity, namely, grade I (intimal tear), grade II (intramural haematoma), grade III (pseudoaneurysm) or grade IV (rupture)[33, 81]. Figure 5 shows the different grades of ATAI severity according to this classification.

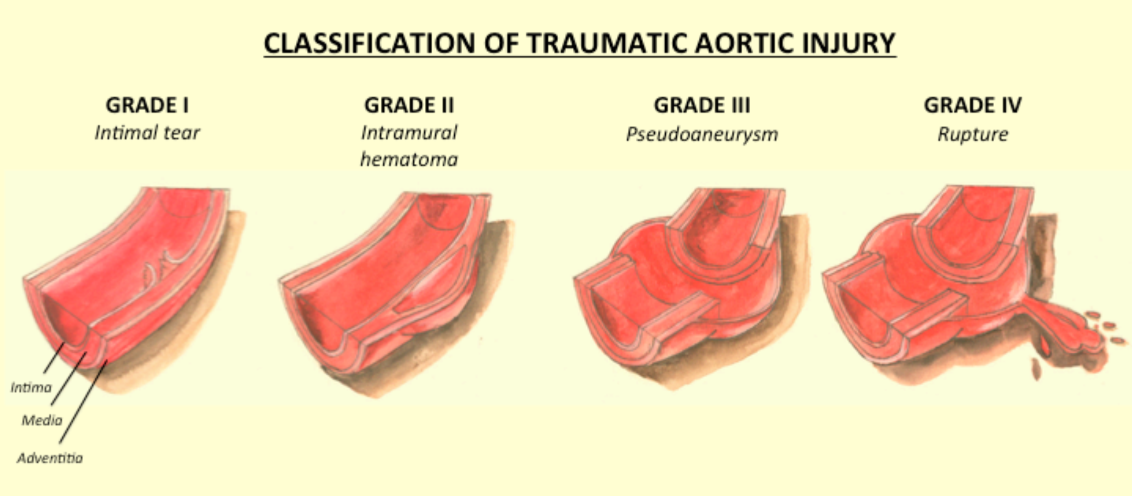


Figure 5. Classification of traumatic aortic injuries proposed by Azizzadeh et al. [33].

Current *Clinical Practice Guidelines of the Society for Vascular Surgery for endovascular repair of traumatic thoracic aortic injury* [81] use this classification to determine whether an aortic injury should be conservatively managed (grades I-II) or whether surgical or endovascular repair is required (grades III-IV).

BRIEF SUMMARY

There are various forms of ATAIs, from limited lacerations of the intima to a complete transection of the aorta. Partial circumferential tears are typical of mild trauma, occur less frequently and are associated with intramural haematomas and focal dissections. In severe cases the tear usually extends into the adventitial layer, leading to a partial or complete transection of the aorta; the latter is associated with a high mortality rate. In contained aortic ruptures, a chronic pseudoaneurysm may develop and cause late symptoms due to the compression of near structures or to rupture.

Several classifications have been proposed based on imaging, surgical and autopsy findings. Most injuries occur at the aortic isthmus, just distal to the left subclavian artery, followed by, in order of decreasing frequency, the ascending aorta, the aortic arch, the distal descending aorta and the abdominal aorta. Non-isthmus aortic injuries and multiple aortic injuries are more frequent in autopsy studies than in clinical practice, suggesting that both situations involve a worse prognosis than isolated ATAIs at the isthmus.

2.5. Clinical signs and symptoms

The presentation of ATAIs may be subtle in some patients. An ATAI manifests in the form of specific signs or symptoms in fewer than 50% of cases [17, 82, 83], whereas the remaining patients have no clinical signs of aortic injury until the sudden onset of haemodynamic instability [60]. Patients may develop dyspnoea, back pain or differential blood pressure in the lower extremities compared to the upper extremities [84-86].

Sturm et al. [85] compared the clinical signs and symptoms of 50 major trauma patients with associated ATAIs with 50 major trauma patients without aortic injury. Each patient's chart was evaluated for chest pain, respiratory distress, thoracic back pain, hypotension, hypertension or a decreased femoral pulse. None of the symptoms or signs reached statistical significance between the groups, indicating that the diagnosis of ATAI cannot be accurately predicted or excluded on the basis of patients' presenting with particular complaints or physical findings [85].

However, a risk assessment for aortic injury can be performed on the basis of the presence of certain clinical variables. Blackmore et al. [87] found that seven criteria were predictors of ATAI: age older than 50 years, being unrestrained, hypotension with a systolic blood pressure of less than 90 mm Hg, thoracic injury, abdominopelvic injury requiring emergent laparotomy or fractures of the lumbar spine and pelvis, long bone fractures and major head injury. It was found that patients who met more of these criteria had a greater chance of having an ATAI and that those who met four criteria or more had a 30% chance of sustaining an ATAI [87]. In a more recent re-evaluation [88] of these clinical predictors, Kirkham et al. reported that only four factors (abdominopelvic injury, thoracic injury, hypotension and being unrestrained) were predictive. These authors concluded that the clinical prediction rule had not been able to stratify the patients into a clinically useful range of injury probabilities, and thus that the prediction rule could not be used to improve the efficiency of the existing detection algorithm [88].

Finding a presternal contusion upon physical examination is strongly suggestive of an ATAI, but this has only been noted in 12% to 43% of trauma patients sustaining an ATAI [85, 89]. A precordial or interscapular systolic murmur (in 14% of patients) or a decrease in the femoral pulse (4%) are also reasonably specific for the presence of an ATAI, but both are too rare to be of significant value [85, 89]. Symbas et al. [90] described the equally rare acute post-traumatic coarctation syndrome, in which blood pressure and pulse amplitude are increased in the upper extremities in addition to a decreased femoral pulse.

BRIEF SUMMARY

An ATAI presents in the form of specific signs or symptoms in fewer than 50% of cases, whereas the remaining patients have no clinical signs of aortic injury until the sudden onset of haemodynamic instability.

A presternal contusion may be found on physical examination, along with a precordial or interscapular systolic murmur or a decrease in the femoral pulse. Post-traumatic coarctation syndrome consists of an increase in blood pressure and pulse amplitude in the upper extremities, in addition to a decreased femoral pulse.

2.6. Radiographic diagnosis of ATAI

2.6.1. Chest X-ray

In the acute trauma setting a supine chest X-ray (CXR) is mandatory. The CXR may be abnormal in major trauma patients with associated ATAIs, but these abnormalities can vary. The predominant rationale for obtaining a CXR in the acute trauma setting is to determine whether or not there are immediate life-threatening lesions that require immediate treatment (massive hemothorax or tension pneumothorax). However, it may also provide information regarding a suspected ATAI. The main goal of the initial chest radiograph is to look for a mediastinal haematoma, and thus a major vascular injury. While a mediastinal width (MW) of greater than 8 cm and/or 25% of the width of the thorax is the most frequent observation, it is not necessarily the most sensitive finding [25, 91-93]. A retrospective study conducted by Wong et al. [94] concluded that both a left mediastinal width (LMW) of 6 cm or more and a mediastinal width ratio (MWR) of 0.60 or more are better radiographic criteria than an MW of 8 cm or more for predicting an ATAI. The authors recommended that major trauma patients with positive test results based on the combined LMW and MWR criteria should proceed immediately to aortography or computed tomography [94]. More discriminatory findings include any abnormality of the transverse aortic arch or a loss of the aortopulmonary window [95, 96].

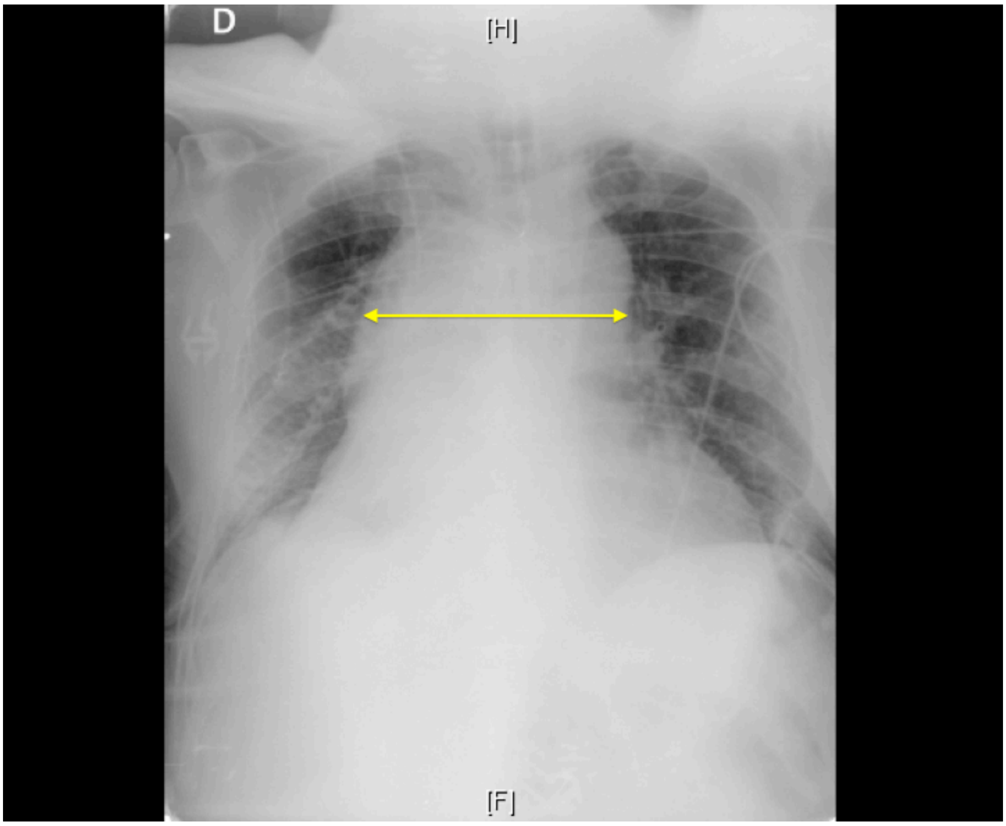


Figure 6. Findings of ATAI on admission CXR I. Supine anteroposterior CXR following MVC shows widening of the mediastinum (arrow).

In 1990, Woodring [97] published a review of 52 articles including 656 patients with ATAI or traumatic injury of the brachiocephalic arteries; 92.7% of the patients had an abnormal mediastinum on the initial chest radiographs obtained in the emergency department, thus enabling the early detection of vascular injury. However, 7.3% of these patients had a normal mediastinum on their initial chest radiographs. The author surmised that this situation occurs when the traumatic pseudoaneurysm is not accompanied by associated mediastinal haemorrhaging or haematoma formation, and where the pseudoaneurysm is either small or is situated in such a way that it does not alter the mediastinal contours. Therefore, the use of accessory clinical and radiographic signs to indicate the need for aortography would have enabled the early detection of an additional 5.6% of the reported cases [97]. Evidence in the literature suggests that the evaluation of serial chest radiographs taken at frequent intervals during the first month following trauma to check for the development of mediastinal abnormalities or a large haemothorax is an acceptable alternative to the routine performance of aortography in blunt chest trauma victims with no clinical or radiographic suspicions of vascular injury. Thus, in the setting of a rapid deceleration force or high clinical suspicion of ATAIs, further investigations are warranted regardless of the findings of chest radiographs [25].

Given that disruption of the aorta requires high-force trauma, other injuries are often present, such as lung (pulmonary contusion), pleura (hemothorax and pneumothorax), diaphragm and thoracic skeletal injuries. Although it has been generally accepted that the presence of thoracic skeletal injuries has a predictive value for the diagnosis of ATAIs, Lee et al. [98] reviewed the initial chest radiographs of 548 patients who had undergone aortography for a suspected ATAI for thoracic skeletal injuries and found that rib fracture was the only thoracic skeletal injury with an incidence significantly higher in patients with ATAI (58.1%) than in those without an ATAI (42.6%) ($P = 0.02$). However, the authors found that the positive predictive value of rib fractures in evaluating ATAIs was 14.8%, and 57.4% the specificity. Therefore, the authors concluded that there was no clinically relevant correlation between thoracic skeletal injuries and ATAIs [98].

Kram et al. [93] reported the following as radiographic indicators for aortography: a paratracheal stripe greater than 5 mm, rightward deviation of the nasogastric tube or central venous pressure line, blurring of the aortic knob and an abnormal or absent paraspinous stripe. The authors found that upper rib fractures and mediastinal to thoracic cage width ratios at any level did not increase the diagnostic accuracy of thoracic aortic rupture.

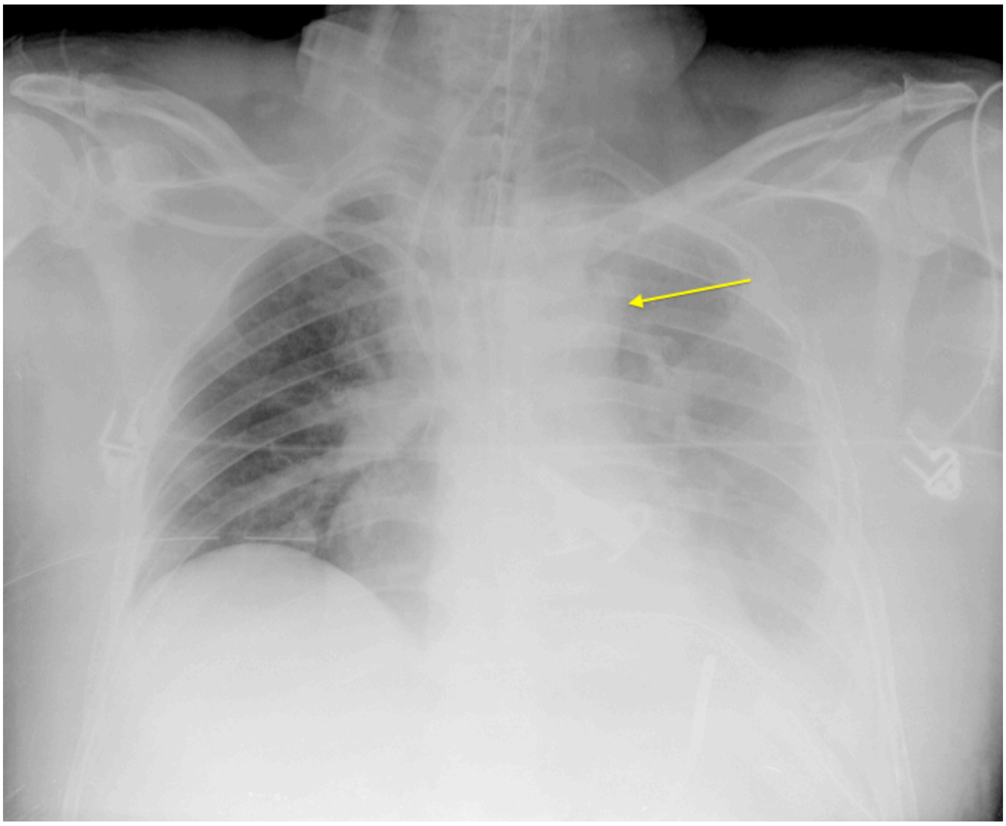


Figure 7. Findings of ATAI on admission CXR II. While width of the mediastinum is difficult to evaluate, the supine anteroposterior CXR following MCC shows blurring of the aortic knob (arrow) and left apical cap.

Other signs of ATAIs on CXR include rightward tracheal, oesophageal, and/or nasogastric tube deviation; left mainstem bronchus depression; and a left apical cap [96, 97, 99].

In 2001, Cook et al. [100] reviewed the CXR of 188 consecutive major trauma patients with suspected ATAIs and only confirmed 10 aortic injuries by aortography. The authors reported the presence or absence of 15 radiographic findings and determined the sensitivity and specificity of individual radiographic signs and combinations of signs; the chest radiograph findings for ATAIs in this study are summarized in Table 6 [100].

CHEST RADIOGRAPH SIGNS†
1. Widened mediastinum (>8.0 cm)
2. Mediastinum-to-chest width ratio greater than 0.25
3. Rightward deviation of the tracheal
4. Blurring of the aortic contour
5. Loss of the aortic knob
6. Left apical pleural cap
7. Depression of the left mainstem bronchus
8. Opacification of the aortopulmonary window
9. Rightward deviation of the nasogastric tube
10. Wide paraspinal lines
11. First rib fracture
12. Other rib fractures
13. Clavicle fracture
14. Pulmonary contusion
15. Thoracic spine fracture

Table 6. Chest radiograph findings associated with ATAIs.

†Data from Cook et al. [100].

Regardless, the greater the degree of manifestation of blunt force trauma, the higher the suspicion should be for ATAI. An abnormal (even minimally so) supine anteroposterior radiograph after trauma should always be accompanied by further imaging.

It should also be emphasized that the most important observation is a clear visualization of the aortic arch, not the absence of mediastinal widening, as a discriminatory feature.

On the other hand, although combining the most sensitive CXR signs may improve sensitivity up to 90% in certain series, there is a simultaneous decrease in specificity (even <50%) which fails to provide a sufficient negative predictive value [60, 100]. In addition, it has been reported in the literature that up to 30% of patients with ATAIs may not present mediastinal abnormalities [97]. The vast majority of major trauma patients had a CXR taken in the supine position using portable imaging equipment. Thus, in a significant number of cases, the interpretation of CXR findings in major trauma patients may be difficult due to the poorer technical quality of supine radiographs taken using portable equipment [92, 100].

2.6.2. Computed tomography scan

The use of computed tomography (CT) for the diagnosis of traumatic aortic and major arterial branch vessel injury has evolved significantly over the last three decades. In the early 1980s, reports began to appear describing this CT application and some early series indicated that this method was highly accurate for diagnosing or excluding this potentially fatal injury [95, 101-103]. The first CT findings of an injured aorta were a false aneurysm, linear lucency within the opacified aortic lumen caused by the torn edge of the aortic wall, marginal irregularity of the opacified aortic lumen, periaortic or intramural aortic haematoma and dissection [101]. However, not all studies indicated a high level of reliability for CT [104], and some authors even posed a word of caution about the use of CT for screening ATAIs in blunt trauma [105]. In 1994, Durham et al. [104] reported a combined sensitivity of CT for detecting ATAIs in 155 major trauma patients of 88%; the specificity was 54%; the positive predictive value was 9% and the negative predictive value 99%.

As CT technology advanced, first with the introduction of helical CT and later with multidetector CT (MDCT), the quality of images obtained in the axial plane, multiplanar reformations and surface contour and volume rendering techniques improved in parallel [10, 11, 60, 106, 107]. Computed tomography scanning has superseded aortography as the diagnostic modality of choice, with sensitivity and negative predictive values approaching 100% [10, 11, 60, 106-108]. In addition to a superb diagnostic accuracy, other advantages of CT include widespread availability, speed and reasonable costs. Unlike other diagnostic modalities, CT has the unique ability to readily identify associated injuries by scanning the brain, facial bones, neck, chest, abdomen and pelvis in the same diagnostic setting.

When the presence of mediastinal haematomas alone is included as a diagnostic criterion, the number of false-positive findings is high and therefore this should not be used as a criterion for definitive injury, whereas if only direct signs are used the specificity raises to nearly 100% to the detriment of sensitivity [12, 109, 110].

Computed tomography identifies direct signs of aortic injury such as contrast extravasation, intimal flaps, pseudoaneurysm formation, abnormal aortic contours, sudden changes in aortic calibre (“pseudocoarctation”) and filling defects, such as a mural thrombus. The active extravasation of contrast material in practice is exceedingly rare as it often portends impending exsanguination.

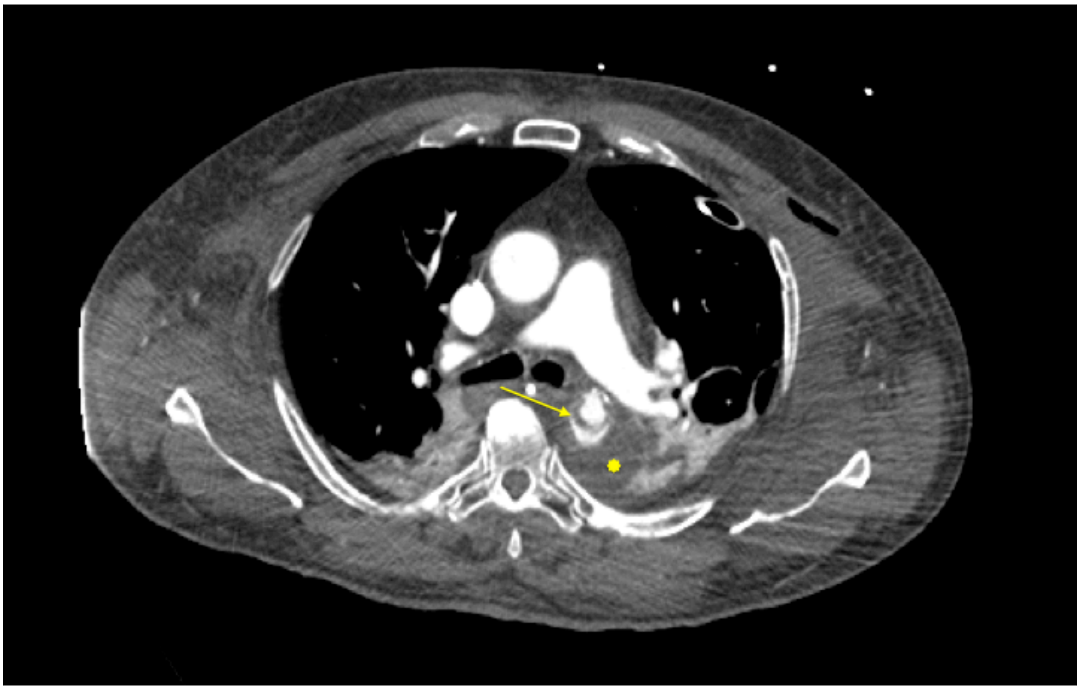


Figure 8. Findings of ATAI in MDCT (I). A 70-year-old male after an MVC presented critical hypoperfusion in the lower body and lack of pulses in both legs. Notice the important periaortic haematoma (asterisk) and the "target-like" injury of the aorta (arrow) at the level of the aortic isthmus, which led to the diagnosis of a "pseudocoarctation syndrome".

The indirect signs of ATAI include periaortic and mediastinal haematomas [109, 111]. As has been mentioned in previous chapters, the most frequent location of an ATAI is the isthmus and the severity of injury at this level can range from minimal intimal injury to a frank rupture with active extravasation. On axial images, these isthmus injuries are most commonly observed along the medial curvature of the arch at the level of the left pulmonary artery and left mainstem bronchus and should be the first location the radiologist looks at when encountering a large mediastinal haematoma.

The most common indirect sign of an ATAI is periaortic haemorrhaging in direct communication with the aorta. When a fat plane is visible between a mediastinal haematoma and the aorta there may be venous mediastinal bleeding or bleeding from aortic side branches [10, 60, 107, 112]. A mediastinal haematoma may also be caused by fracture of the sternum or a vertebral body, in which case a fat plane is also usually seen between the haematoma and the aorta. A mediastinal haemorrhage that is isolated in the anterior or posterior mediastinum and is not in direct contact with the aorta is seldom associated with a major arterial injury [10, 113, 114]. In cases of isolated mediastinal haematomas, other possible sources of bleeding should be considered before directing patients to thoracic aortography [114].

Periaortic haematomas can be tracked down to the level of the diaphragm, potentially creating retrocrural haematomas. In patients who have undergone abdominal multidetector CT alone, the presence of a retrocrural haematoma or a small calibre aorta may be an indication of thoracic aortic injury [10]. Wong et al. [115] reported a periaortic haematoma near the diaphragm being a sign of ATAI with a sensitivity of 70%; a specificity of 94%; a positive predictive value of 74%, and a negative predictive value of 92%. The positive likelihood ratio for the presence of aortic injury was 10.8 and the negative likelihood ratio was 0.3. The authors concluded that a periaortic haematoma near the diaphragmatic crura is an insensitive but relatively specific sign of aortic injury after blunt trauma. In the presence of a periaortic haematoma without direct signs of major vessel injury, as would be seen in a technically adequate study, whether or not follow-up scans should be performed within 48-72 h is still under debate [10, 60].

In 2008, Demetriades et al. [78] published a comparison of the two multicentre prospective studies undertaken by the *American Association for the Surgery of Trauma* in 1997 ($AAST_1$) and 2007 ($AAST_2$), and reported a major shift in the diagnosis of aortic injury, with the widespread use of CT scanning and the almost complete elimination of aortography and TEE.

2.6.2.1. CT scan: multidetector computed tomography

The advent of MDCT has revolutionized the diagnostic modality for the initial evaluation of blunt thoracic trauma. Imaging protocols for MDCT evaluation of the thoracic aorta vary considerably depending on the technical specifications of the device (e.g. the number of detector rows, the availability of electrocardiographic gating, etc.) [60, 107]. In general, the axial reconstruction thickness should be between 1 and 3 mm, with 4×2.5 mm collimation on 4-row scanners, 16×1.25 mm (or 1.5mm) on 16-row scanners, 64×0.5 mm on 64-row scanners and 128×0.6 mm on the most recent 128-row scanners [107].

Steenburg et al. reported that MDCT has a sensitivity of 96.0%; a specificity of 99.8%; a positive predictive value of 92.3%; a negative predictive value of 99.9%, and an accuracy of 99.8% in ATAI diagnosis [11]. Besides this, difficult cases can be approached via the interactive manipulation and interpretation of the dataset in order to generate multiplanar reconstructions (MPR) in various obliquities of the coronal and sagittal plane for optimal display of vascular injuries and morphology and location with respect to adjacent vascular structures, such as the left subclavian artery (LSA) [60, 107].

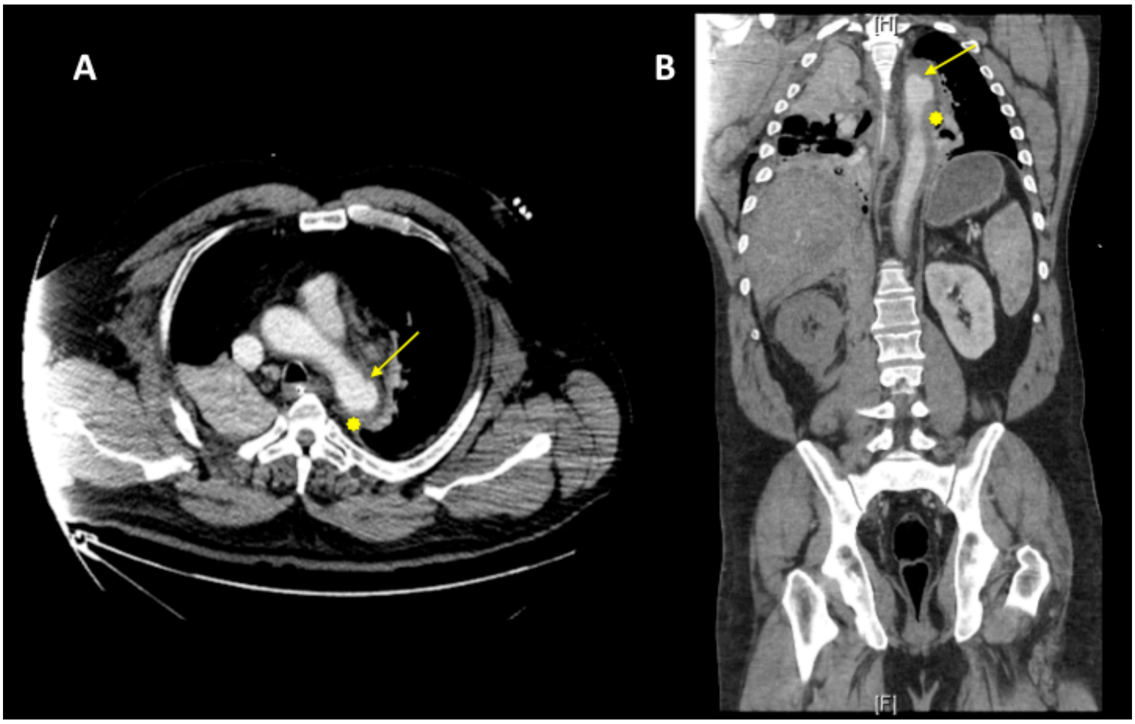


Figure 9. Findings of ATAI in MDCT (II). Focal aortic dissection (arrow) and periaortic haematoma (asterisk) at the level of the aortic isthmus in MDCT images (**A**, axial slice and **B**, coronal reconstruction).

In spite of the fact that direct and indirect findings of ATAI are usually identifiable in axial images, the determination of some complex issues such as the exact morphology and extent of vascular injury may require coronal and sagittal images. Oblique reconstructions resembling the images obtained in conventional angiography, as well as sagittal, coronal and MPRs, should be generated on a 3D Workstation whenever findings are equivocal on axial datasets, necessitating axial reconstructions with one-third (3×2) to one-half (2×1) overlap in scanners of up to 16 detector rows. Due to isotropic voxel datasets in scanners with 64 detector rows or more, overlap in axial reconstructions is not an issue. Furthermore, the MPRs and three-dimensional volume-rendered images obtained from the isotropic datasets acquired by the MDCT may be extremely useful when planning surgical repair, especially endovascular repair.

The improved spatial resolution of the MDCT is currently responsible for the increasingly frequent diagnosis of minimal aortic injuries, which only affect the intima of the aortic wall [116]. Malhotra et al. reported an incidence of minimal aortic injuries of up to 10% among 198 blunt trauma patients who were diagnosed by CT scanning and confirmed by aortography with or without intravascular ultrasound (IVUS) [116]. The authors found that aortography was normal in nearly half of the cases in patients with minimal aortic injury, requiring a more invasive diagnosis technique as IVUS or video angiography.

Finally, MDCT has also improved the diagnosis of trauma patients with mediastinal haematoma but without direct signs of aortic injury. Using the volumetric data acquired by MDCT, a careful search for a supra-aortic vessel injury should be performed in the presence of a mediastinal haematoma when there is no direct sign of aortic injury, as well as in any case of ATAI.

2.6.2.2. CT scan: imaging pitfalls

Several anatomical variants can mimic an ATAI, including:

- **Aortic spindle.** The aorta in the new-born is narrowed between the LSA and the ductus arteriosus. This isthmus disappears after 2 months of age due to cessation of flow through the ductus arteriosus and increased flow through the narrowed region. Although this configuration is usually no longer visible in the adult, the region is still referred to as the isthmus. Immediately beyond the ductus arteriosus the aorta presents a fusiform dilation, which His called the "aortic spindle", which is the point of junction of the two parts being marked in the concavity of the arch by an indentation or angle. In the adult, these conditions can persist to some extent, and it has been pointed out that the average diameter of the spindle can exceed that of the isthmus by up to 3 mm [10]. The change in aortic diameter and the slight indentation at the transition can be mistaken for an injury. The MPR along the major axis and endoluminal images verify the integrity of the aortic wall whenever there is doubt.

- **Classic ductus diverticulum.** The ductus diverticulum is the term used for a focal, convex bulge along the anterior undersurface of the isthmic region of the aortic arch. It has been identified by thoracic aortography in 33% of infant patients but only in 9% of adult patients [117]. Usually, the ductus bulge has a smooth contour forming obtuse angles with the aortic lumen without intimal flaps at the junction of the lumen and the focal bulge [118]. In contrast, the typical pseudoaneurysm forms an irregular outpouching from the lumen, often displaying acute margins and intimal irregularity at its base [118].
- **Atypical ductus diverticulum.** Compared with the classic ductus diverticulum, the atypical ductus diverticulum has a somewhat shorter and steeper slope superiorly and a more classic gentle slope inferiorly [118]. Nonetheless, both shoulders have smooth, uninterrupted margins, an important feature that distinguishes this variant from a true injury. The use of endoluminal views and the absence of periaortic mediastinal blood can exclude an intimal injury.
- **Ductus remnant.** A fibrotic remnant of the ductus arteriosus can persist and be observed arising from the aorta upon intravenous contrast-enhanced MDCT studies. The remnant often displays linear calcification

and is thus easy to identify and distinguish from an injury.

- **Branch vessel infundibula.** Infundibula of aortic branch vessels, including the brachiocephalic artery, bronchial artery, intercostal arteries (right third most common), left common carotid artery and LSA, may simulate traumatic aortic injuries. Infundibula typically occur at the origin of these vessels from the aortic arch and they have smooth anatomical margins. This latter characteristic helps differentiate these variants from false aneurysms, which are usually irregular and have sharp, non-anatomical margins [118].

Breathing/pulsation/motion artefacts can also be misinterpreted as being ATAIs. It should also be noted that ATAIs can occur in the absence of a periaortic haematoma and at atypical sites of the aorta.

2.6.2.3. Risks associated to the widespread use of high-resolution CT scans: an increased source of radiation exposure

Various measures are used to describe the radiation dose delivered by CT scanning, the most relevant being absorbed dose, effective dose, and CT dose index. The absorbed dose is the energy absorbed per unit of mass and is measured in grays (Gy). One gray equals 1 joule of radiation energy absorbed per kilogram. The organ dose (or the distribution of dose in the organ) will largely determine the level of risk to that organ from the radiation. The effective dose, expressed in sieverts (Sv), is used for dose distributions that are not homogeneous (which is always the case with CT); it is designed to be proportional to a generic estimate of the overall harm to the patient caused by the radiation exposure. The effective dose allows for a rough comparison between different CT scenarios but provides only an approximate estimate of the true risk. For risk estimation, the organ dose is the preferred measure.

The number of scans in a given study is, of course, an important factor in determining the dose. For example, Mettler et al. [119] reported that in virtually all patients undergoing CT of the abdomen or pelvis, more than one scan was obtained on the same day; among all patients undergoing CT, the authors reported that at least three scans were obtained in 30% of patients, more than five scans in 7%, and nine or more scans in 4%. The radiation doses to particular organs from any given CT study depend on a number of factors. The most important are the number of scans or phases, the tube current and scanning time in milliamp-seconds, the size of the patient, the axial scan range, the scan pitch (the degree of overlap between adjacent CT slices), the tube voltage in the kilovolt peaks and the specific design of the scanner being used [120]. Depending on the machine settings, the organ being studied typically receives a radiation dose in the range of 15-30 millisieverts (mSv) in an adult for a single CT scan, with an average of two to three CT scans per study. At these doses, there is a small but certain risk for radiation-induced carcinogenesis [121]. Indeed, many agitated patients with traumatic injury must undergo successive imaging attempts, and the use of dosimeters on patients during trauma assessment has demonstrated doses far exceeding the initial estimates [122].

Of particular concern with thoracic CT are cancers of the thyroid, breast, and lung, all of which are linked to radiation exposure. A typical patient with traumatic injury who undergoes irradiation at a young age incurs an increased cumulative lifetime risk of developing cancer [123, 124]. A radiation dose of 0.01 Gy raises the risk of breast cancer in a 35-year-old woman by about 14%. The average thoracic CT system delivers at least twice this dose [125].

There is direct evidence from epidemiologic studies that the organ doses corresponding to a common CT study (two or three scans, resulting in a dose in the range of 30 to 90 mSv) result in an increased risk of cancer [123, 124]. In 2005 a large-scale study of 400,000 radiation workers in the nuclear industry [126] who were exposed to an average dose of approximately 20 mSv (a typical organ dose from a single CT scan for an adult) reported a significant association between the radiation dose and mortality from cancer in this cohort (with a significant increase in the risk of cancer among workers who received doses between 5 and 150 mSv).

A 2006 report from the *National Research Council of the National Academies* [127] indicated that previous studies had underestimated the deleterious effects of diagnostic radiation. It was estimated in 2007 that up to 2% of all future cancer cases in the United States might be due to radiation from CT [123, 124].

Concern about excess radiation exposure has given rise to various techniques and technologies designed to minimize radiation exposure [122] none of which are as effective as thoughtfully avoiding non-indicated imaging altogether.

In summary, the potentially detrimental effects of serial high-radiation tests during a long period of time must be weighed up, especially in young patients.

2.6.3. Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has been proven to be remarkably accurate in the detection of ATAIs [128, 129]. Notwithstanding its excellent imaging test properties, MRI actually has few uses in the evaluation of ATAIs because of long examination times and limited access. Conversely, some authors have reported [128-130] that MRI may have a role in follow-up when a delay in surgery is contemplated and minimal or equivocal intimal injuries are present, particularly as a strategy for radiation dose reduction in young trauma victims. Furthermore, considering the fact that more patients are undergoing endovascular repair for ATAIs and that these patients require lifelong imaging surveillance, MRI appears to be a valuable tool for the assessment of thoracic stent grafts [131].

In summary, its ability to provide additional functional information and the lack of ionizing radiation and nephrotoxic contrast agents may make MRI a valuable tool for monitoring patients after endovascular aortic repair [131, 132].

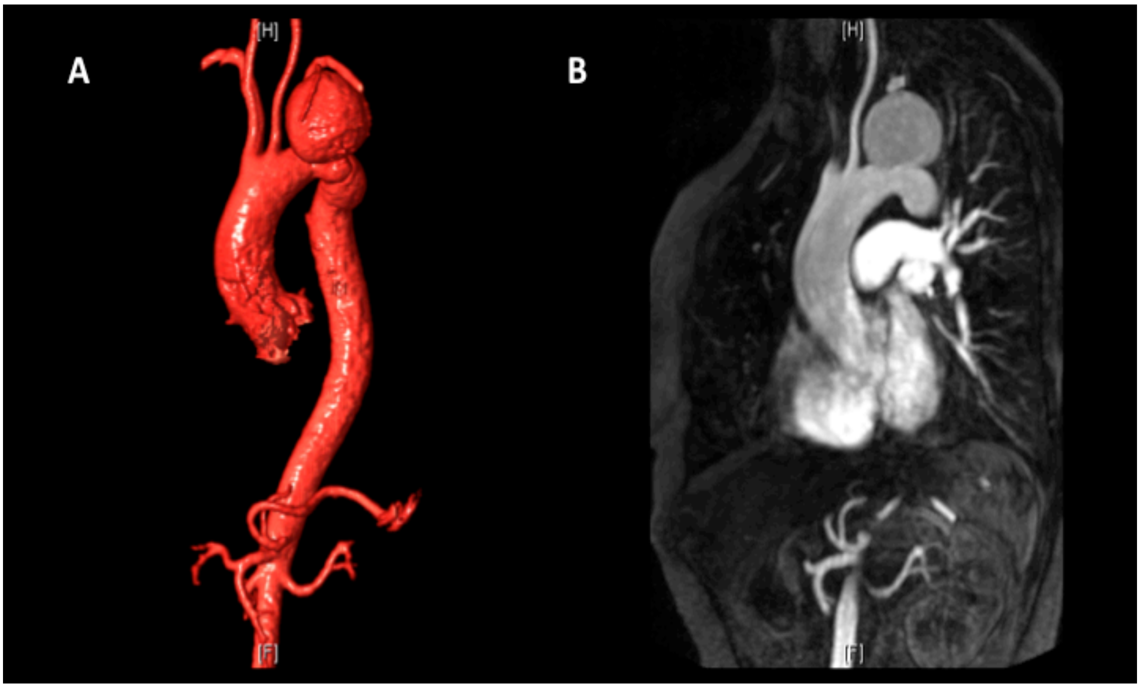


Figure 10. MRI in ATAIs. Control MRI of a saccular post-traumatic pseudoaneurysm in a 51-year-old female 6 years after a fall. **A.** Three-dimensional reconstruction image shows the presence of a huge saccular aneurysm involving the origin of the LSA. **B**. Maximum Intensity Projection revealed compression and displacement of the LSA.

2.6.4. Aortography

Historically, aortography was the gold standard for the diagnosis of aortic injury. However, the procedure is associated with some risk and requires 60 to 70 minutes to perform [104]. Trauma diagnosic thoracic aortography is usually performed with the use of a 5 or 6-French pigtail catheter inserted into the aortic arch by either a femoral approach or, less commonly, a humeral approach [133-137]. Anteroposterior and 45-degree right posterior oblique views are obtained after the administration of 40 to 70 ml of contrast medium, and additional views are acquired as needed.

The role of aortography has traditionally been to identify or exclude ATAI and, if present, determine the exact location of the injury with respect to the branch vessels and to evaluate for co-existing branch vessel injuries [134, 135]. The thoracic aorta must be assessed for evidence of an intraluminal flap (filling defect), extravasation of dye (pseudoaneurysm) or an abnormal contour of the aortic wall (intramural haematoma) [136-138].

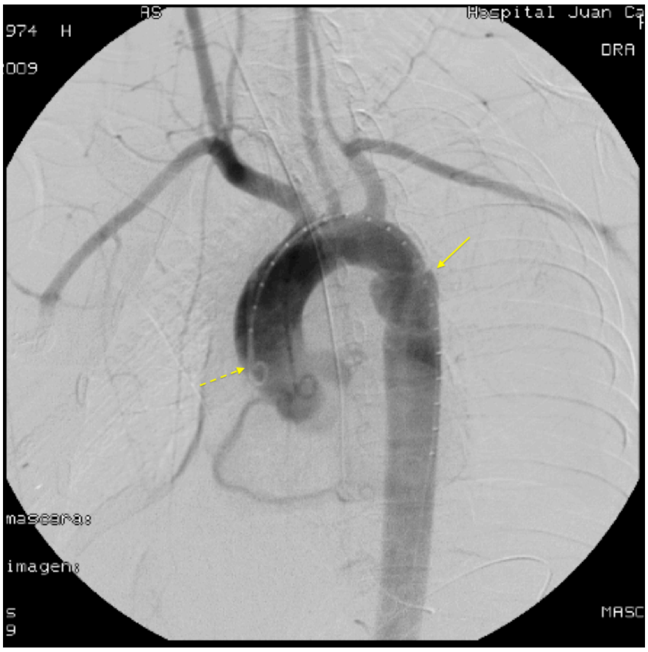


Figure 11. Aortography (I). Emergent aortography confirming a traumatic aortic

transection of the descending aorta (solid arrow). Notice the diagnostic 6 French pigtail catheter in the ascending aorta (dashed arrow).

The value of conventional aortography for the evaluation of ATAI is well established, with a sensitivity of nearly 100%, a specificity of more than 98% and an accuracy of more than 99% [60, 104, 139-141]. Besides, false-positives and false negatives are as low as 1-2% [104, 141].

One of the disadvantages of aortography is the need for a skilled team to perform the study. On the other hand, the majority (85%-95%) of these diagnostic aortographies are negative [93, 134, 142]. In addition, the rates of contrast reactions, contrast-induced nephropathy, groin haematomas, aortic intimal tears from angiographic catheters and pseudoaneurysm formation are low but not negligible. Sturm et al. reported a complication rate of 1.7% when performing diagnostic aortography in blunt trauma patients [134].

Figure 12. Aortography (II). Emergent aortography reveals a focal outpunching

(arrow) at the ligamentum arteriosum caused by a fall.

In spite of its potential complications and the better accuracy of the MDCT scan, the performance of an intraoperative aortography is mandatory prior to the deployment of a thoracic aortic endograft. Moreover, the role of aortography in the embolization and/or stenting of bleeding branch vessel associated with an ATAI is of a paramount importance [137].

2.6.5. Intravascular ultrasound

Intravascular ultrasound (IVUS) is another useful adjunctive imaging modality that can be used to provide high-resolution cross-sectional images of the vessel wall and the surrounding tissues. The potential findings of an aortic injury during IVUS include vessel wall disruption, intimal flap, focal pseudoaneurysm, intramural and periaortic haematoma and complete transection [143-146].

The intact wall of the aorta has a three-layered appearance (hyperechoic inner layer, hypoechoic middle layer and hyperechoic outer layer that blends with the periaortic tissue). Any disruption in the integrity of the aortic wall is readily detected by intravascular sonography [145, 146]. Blurring of the layered appearance may be caused by an intramural haematoma. Floating intimal flaps are often visible moving in the aortic lumen. In aortic dissection, the pulsatile membrane is usually oriented in a concave manner towards the false lumen and the outer wall of the false lumen shows a single hyperechoic layer that blends with the hyperechoic periadventitial tissue [147]. A pseudoaneurysm of the aortic wall presents as a hypoechoic bulging structure beyond the limits of the aortic contours, in continuity with the aortic lumen and associated with a hyperechoic flap containing the intima and media. Increased echogenicity of the surrounding tissues is suggestive of periaortic haematoma, but periaortic haematoma is not easily identified by intravascular sonography [147].

Although these findings are considered to be specific for ATAI, false-positive results have been described [145, 146]. The advantages of IVUS mainly involve its problem-solving capabilities. It can be performed alongside conventional aortography and has been shown to be a useful complementary modality [143, 144]. Patel et al. published a prospective series of 14 consecutive major trauma patients with abnormal aortography findings who were undergoing a complementary IVUS study [146]. The authors reported 11 true positives, 2 true negatives and 1 false negative, resulting in 91.7% sensitivity and a nearly 100% specificity [146].

One of the main drawbacks of IVUS is its inability to provide a complete and expeditious survey of the aorta and brachiocephalic arteries [143, 144]. Moreover, IVUS is an operator- and experience-dependent invasive procedure, requiring arterial puncture [143, 144]. Technical limitations of IVUS, such as the depth of penetration, also exist and are inherent in the size and frequency of the ultrasound transducer [145]. In addition, some anatomical abnormalities, such as an atypical ductus diverticulum, may be mistakenly interpreted as a sign of traumatic injury of the aorta by IVUS [145], requiring further studies.

On the other hand, IVUS provides immediate and dynamic imaging of aortic pathology, which can be helpful in treating aortic pathology [148]. Intravascular ultrasound has been shown to reduce the need for contrast imaging during endovascular aortic repair. Some authors have surmised that the use of IVUS during endovascular aortic repair to reduce contrast load, fluoroscopy time and complications can ultimately improve patient outcomes [148-150].

2.6.6. Transesophageal echocardiography

The speed and portability of transesophageal echocardiography (TEE), combined with the ability to obtain high-resolution images of the aorta, make it an attractive diagnostic modality [151]. In addition, TEE can be performed without interrupting ongoing measures to stabilize the trauma patient. Consequently, TEE has been routinely performed in victims of violent deceleration collisions, even in patients presenting an apparently normal mediastinum on supine chest radiography [152].

In 1997, Goarin et al. [153] published a prospective study describing the signs on TEE associated with ATAI. Twenty-eight patients with ATAI underwent TEE and were compared with a control group of 30 thoracic trauma patients without aortic injury. The TEE signs were classified as direct or indirect signs. The most frequent direct sign was thick stripes, followed, in decreasing order, by free-edge intimal flaps, fusiform aneurysms, false aneurysms, aortic dissections, aortic wall haematomas and complete aortic obstruction. The indirect signs included minor increases in aortic diameter, impairment of the aortic Doppler colour flow and an increase in the aorta-probe distance, indicating hemomediastinum [153]. The authors found significant blurring of the aortic outline in 20% of cases and intraluminal artefacts in 36% of cases, but none of that signs seemed to impair an accurate diagnosis of ATAI. Transesophageal echocardiography even allowed a diagnosis of limited intimal lesions, which is frequently missed by other conventional methods [153]. It also permitted a rapid diagnosis of complete rupture, in which fast degeneration means that more time-consuming methods are not practical [153]. Several investigators reported traumatic aortic injuries in the form of thick protruding membranes and mural or medial flaps [80, 151].

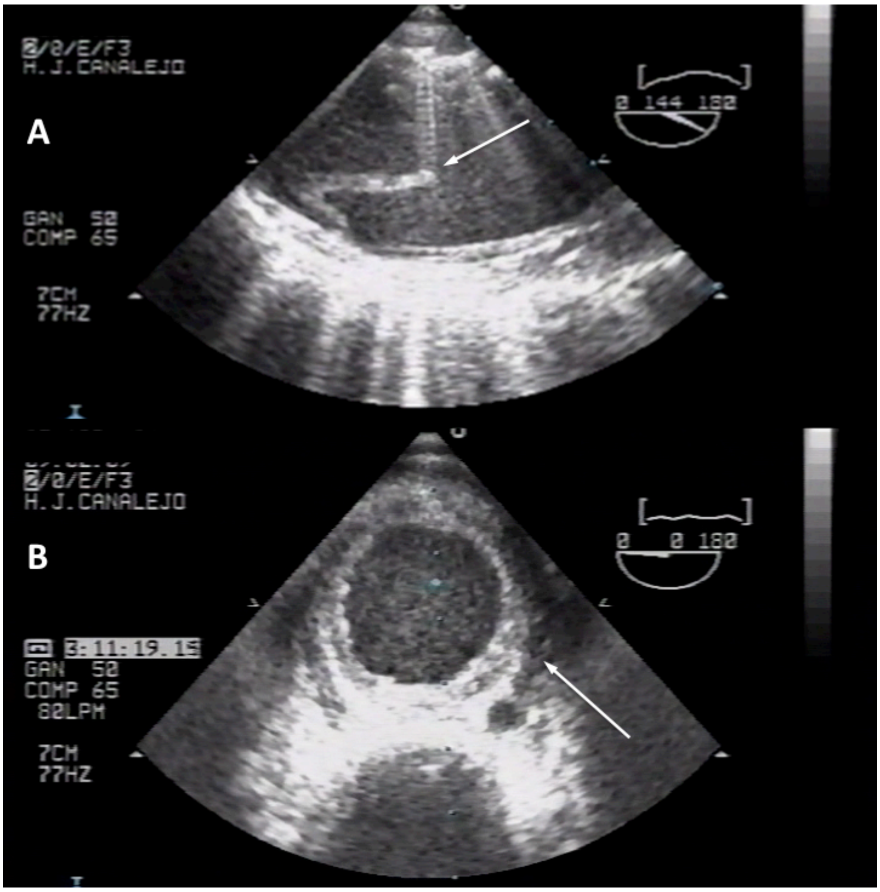


Figure 13. TEE in ATAIs. A. Biplane TEE in the longitudinal plane of the proximal descending aorta showing a traumatic intimal flap (arrow). **B.** Biplane TEE in the axial plane of the mid-descending aorta presenting a significant periaortic hematoma (arrow).

Changes in the shape of the aorta have also been frequently detected by TEE in patients with ATAI [153-155]. The most typical echocardiographic abnormality is a localized distortion in the circular area of the aorta due to a pseudoaneurysm. A less common but highly suggestive finding revealed by TEE is fusiform dilation, with the diameter of the disrupted portion of the thoracic aorta measuring ≥ 1.5 times more than that of the uninvolved aorta.

Transesophageal echocardiography may also be useful in the quantification of traumatic hemomediastinum [156, 157]. Le Bret et al. described three different TEE signs of mediastinal haematoma: an increased distance between the probe and the aortic wall, a double contour of the aortic wall, and visualization of the ultrasound signal between the aortic wall and the visceral pleura [156]. The authors also found that the distance between the oesophageal probe and the aortic wall was the most accurate sign because it could be easily obtained; the threshold value for this distance was 3 mm [156]. Furthermore, in 1998, Vignon et al. [157] established that the presence of hemomediastinum may be quantitatively assessed by two measures: the distance between the oesophageal probe and the anteromedial aortic wall, and the distance between the posterolateral aortic wall and the left visceral pleura at the level of the aortic isthmus. The investigators also determined a threshold value of 5.5 mm for the distance between the oesophageal probe and the anteromedial aortic wall, and 6.6 mm between the oesophageal probe and the posterolateral aortic wall and the left visceral pleura. Those signs had a sensitivity of 80%, a specificity of 92% and a positive and negative predictive value of 86% and 89%, respectively, for the diagnosis of underlying major vascular injury [157].

Vignon et al. [80] proposed a new classification of ATAIs into four types based on TEE features and combining the anatomical classification of Parmley et al. [2]. The first type of ATAI in their schema is the traumatic aortic intimal tears. These are superficial lacerations of the intima that do not involve the media or adventitia and are often only detectable by TEE. On TEE imaging they appear as mobile, thin, linear echo densities that are attached to the inner surface of the aortic wall. The second type of lesion, which is the partial subadventitial aortic disruption, is in the form of deep tears in the media without extensive circumferential separation of the layers of the aortic wall. This appears as a deep break in the continuity of the aortic wall, as revealed by TEE, usually without an associated flap. The subtotal subadventitial aortic disruption is the third type of injury and is characterized by a tear that involves at least two thirds of the aortic circumference. The aortic wall is held together by a small section of intact media and adventitia. The pathognomonic feature on TEE is a thick linear flap that traverses the lumen of the aorta obliquely or transversely in the transverse plane and vertically in longitudinal images, while usually remaining nearly perpendicular to the wall of the descending aorta. In the last type, the complete subadventitial aortic disruption, the media is completely separated from the adventitia along the entire circumference of the aorta. Its appearance on TEE is a thick circular flap lying within the aorta. This classification method has prognostic value because all of these injuries, except traumatic aortic intimal tears, require surgical management [80].

The sensitivity of TEE for diagnosing ATAIs ranges from 57 to 100%, whereas the specificity ranges from 84 to 100% [80, 151, 158-160]. The reason for the great variability in the reported sensitivity and specificity values is that TEE is an operator- and experience-dependent procedure. Indeed, some authors reported a sensitivity and specificity of TEE of 57% and 91% compared with a sensitivity and specificity of aortography of 89% and 100%, respectively, within the same series [159].

Besides imaging ATAIs, TEE is an invaluable tool in the evaluation of all cardiovascular abnormalities in chest trauma patients, such as myocardial contusion, pericardial effusion, valvular abnormalities and hypovolemia. Transesophageal echocardiography may be especially useful for providing a safe and rapid method for examining mediastinal structures and evaluating the hemodynamic status of intubated major trauma patients, as reported by Catoire et al. [161]. The authors found that a TEE systematic evaluation of major trauma patients revealed up to a 70% of cardiovascular diagnoses [161]. Likewise, Karalis et al. carried out a prospective study to provide a complete echocardiographic assessment of cardiac structure and function [158]. The investigators used echocardiography to diagnose a myocardial contusion in 30% of patients, and severe right ventricular dysfunction as the cause of hypotension in 1.9% of cases [158]. In 1998, García-Fernández et al. [162] published a multicentre trial designed to evaluate the usefulness of TEE for detecting cardiac damage after blunt chest trauma and to compare the findings of TEE with those provided by the electrocardiogram and cardiac isoenzymes assay. Relative to pathological TEE findings, the sensitivity and specificity of an abnormal electrocardiogram were 59% and 73%, respectively, whereas a high CK-MB with CK-MB/CK > 5% presented a sensitivity and specificity of 64% and 52%, respectively. The authors concluded that TEE can be routinely used to diagnose cardiac injuries, whereas electrocardiogram and isoenzyme assays are not good methods for detecting cardiac damage after a blunt chest trauma [162].

One of the main drawbacks of TEE is its inability to consistently image the distal ascending aorta and aortic arch branches, which can be injured by severe blunt chest trauma. Ahrar et al. [135] conducted a retrospective study of 89 cases of ATAI documented by angiography that showed injuries in the distal ascending aorta and aortic branches that would not have been detected by TEE in 20% of the patients. Other authors [154] similarly pointed out the limitations of TEE for the diagnosis of traumatic injuries to aortic branches.

In conclusion, TEE has a role in major trauma patients as an intermediate screening test for ATAIs, especially in intubated and/or haemodynamically unstable patients, before proceeding to aortography or CT scanning, as well as being the main test for assessing the presence of concomitant cardiac injuries.

BRIEF SUMMARY

In the acute trauma setting, the supine chest X-ray (CXR) is of paramount importance. An abnormal supine anteroposterior CXR in trauma should always be evaluated with further imaging. A mediastinal widening greater than 8 cm and/or 25% of the width of the thorax is the most frequent observation, whereas both a left mediastinal width ≥6 cm and a mediastinal width ratio ≥0.60 present a higher sensitivity. Other signs of ATAI on CXR include any abnormality of the transverse aortic arch; loss of the aortopulmonary window; rightwards tracheal, esophageal and/or nasogastric tube deviation; left mainstem bronchus depression, and a left apical cap.

Nowadays, multidetector CT (MDCT) has superseded aortography as the diagnostic modality of choice, with sensitivity and negative predictive values approaching 100%. Other advantages of CT include its widespread availability, speed, reasonable costs and the ability to readily identify associated injuries. Direct signs of ATAI on CT include contrast extravasation, intimal flaps, pseudoaneurysm formation, abnormal aortic contour, sudden change in aortic calibre (“pseudocoarctation”) and filling defects. Indirect signs of ATAI are periaortic haemorrhage and mediastinal haematomas. In complex cases a diagnosis can be reached thanks to oblique reconstructions, which resemble the images obtained in conventional angiography, as well as the sagittal, coronal and multiplanar reconstructions provided by MDCT.

Magnetic resonance imaging has little use in the evaluation of ATAIs, despite its high degree of accuracy, because of long examination times and limited access. Magnetic resonance imaging has a role in follow-up when delayed surgery or non-operative management is selected, as well as in lifelong imaging surveillance after aortic endografting, as a strategy for radiation dose reduction in young trauma patients.

The role of aortography has traditionally been to identify or rule out an ATAI, to determine the exact location of the injury with respect to the branch vessels and the presence of any co-existing branch vessel injuries. Signs of ATAI are intraluminal flap (filling defect), extravasation of dye (pseudoaneurysm) and abnormal contours of the aortic wall (intramural haematoma). Aortography for the evaluation of ATAI presents a sensitivity of nearly 100% and a specificity > 98%. Disadvantages of aortography include the need for a skilled team, contrast reactions, contrast-induced nephropathy, groin haematomas, aortic intimal tears from catheters and pseudoaneurysm formation. Intraoperative aortography is still mandatory prior to the endovascular repair of ATAI.

Intravascular ultrasound (IVUS) is a useful complementary modality to aortography that provides immediate and dynamic imaging of aortic pathology and reduces contrast load, fluoroscopy time and complications during endovascular aortic repair. The drawbacks of IVUS include its inability to provide a complete survey of the aorta and brachiocephalic arteries and the fact that it is an operator- and experience-dependent invasive procedure. Periaortic haematomas are not easily identified by IVUS.

The sensitivity of transesophageal echocardiography (TEE) for diagnosing ATAIs ranges from 57% to 100% and the specificity from 84% to 100%. Its advantages are speed and portability, the acquisition of high-resolution images of the aorta and the assessment of cardiovascular status. Direct signs are thick stripes, free-edge intimal flaps, fusiform and false aneurysms, aortic dissection, wall haematomas, and complete aortic obstruction. Indirect signs include changes in aortic diameter, impairment of the aortic Doppler colour flow and an increase in aorta-probe distance, indicating hemomediastinum. The disadvantages are the fact that it is an operator- and experience-dependent test and its inability to image the distal ascending aorta and arch branches.

2.7. Management of ATAIs

The treatment of ATAIs in major trauma patients has traditionally posed a surgical challenge because of several reasons, namely, the initial delay in diagnosis in large numbers of patients, the high rates of morbidity and mortality due to associated non-mediastinal injures, and the potential surgery-related complications.

As with any trauma patient, the initial assessment begins with principles of the *Advanced Trauma Life Support* protocol. This includes a rapid assessment of airway, breathing and circulation, followed by a thorough secondary survey that includes obtaining adjunctive laboratory and radiographic data. In unstable patients, the repair of a contained aortic rupture is third in the hierarchy of addressing life-threatening injuries. Ongoing haemorrhaging must be controlled first, regardless of the source. This may include chest tube drainage of a hemopneumothorax, temporary stabilization of long-bone fractures, temporary stabilization of unstable pelvic injuries, exploratory laparotomy or thoracotomy, and coil embolization of ongoing pelvic bleeding. Secondly, intracranial haemorrhaging causing a mass effect must be identified and drained. Aortic injuries should be subsequently addressed. Ongoing resuscitation should continue and beta-blocker therapy should be instituted as dictated by the patient's haemodynamic status in preparation for definitive treatment of the aortic injury [67]. Historically, open repair via thoracotomy has been the standard to which all other management strategies were compared. Conventional open repair of ATAIs via the interposition of a graft for replacing the injured segment is a safe, effective and durable technique. However, as endovascular strategies for treating abdominal and, more recently, thoracic aortic pathologies have evolved, there is growing enthusiasm for thoracic endovascular aortic repair (TEVAR) of ATAIs because of its relative ease, reduced operative time, and potentially decreased complication rate compared to conventional open repair.

2.7.1. Medical treatment

When a presumptive diagnosis of ATAI is made, haemodynamic monitoring and medical therapy should be initiated before a definitive imaging test is performed (CT, aortography, TEE). Aortic wall stress is affected by the velocity of ventricular contraction (dP/dt), the rate of ventricular contraction and blood pressure. Medical therapy should include intravenous infusion of a vasodilator to avoid hypertension and the limitation of intravenous fluid infusion once the systolic arterial pressure exceeds 100 mmHg. Initial medical stabilization using beta-blockers controls these three parameters by reducing heart rate and blood pressure as much as possible whilst still maintaining adequate end-organ perfusion [14]. The systolic blood pressure should be titrated to approximately 100 mmHg and the heart rate to <60 bpm [12-14]. The first-line medical treatment for ATAIs recommended by current *ACCF/ AHA/ AATS/ ACR/ ASA/ SCA/ SCAI/ SIR/ STS/ SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease* is intravenous propranolol, metoprolol, labetalol or esmolol [163]. In patients who have a potential contraindication to beta blockade, esmolol may be a viable option given its extremely short half-life. Use of labetalol, which is both an alpha- and beta-receptor antagonist, offers the advantage of adequate heart rate and blood pressure control from a single agent, potentially eliminating the need for a secondary vasodilator. In patients who are unable to tolerate beta blockade, nondihydropyridine calcium channel antagonists (verapamil, diltiazem) are acceptable alternatives [163]. This therapy should be continued while diagnostic studies and any surgical procedures, if indicated, are being performed [13]. A pulmonary artery catheter can be placed in patients with proven ATAIs who require sustained therapy to maintain a mixed venous oxygen saturation of 65% [12]. This practice may only deviate in the respect that patients with evidence of increased intracranial pressure must be considered immediate operative candidates if other factors permit in order to prevent secondary brain injury associated with the decrease in cerebral perfusion pressure that accompanies hypotensive medical therapy [32].

Warren et al. [164] conducted a study of 37 ATAI patients retrospectively divided into three groups, namely, Group 1 (15 patients without preoperative antihypertensive therapy), Group 2 (15 patients treated for 2 to 7 hours before surgery with antihypertensives) and Group 3 (seven patients treated with antihypertensives for 24 hours to 4 months before surgery to allow recovery from associated severe injuries). The mortality rate was 13%, 7% and 14%, respectively. The authors found that temporary antihypertensive therapy is safe and effective in patients with ATAIs [164]. Subsequently, Pate et al. [13] found that patients with ATAIs at the isthmus, who had not exsanguinated into the pleural cavity upon presentation to hospital, were unlikely to develop a rupture of the haematoma during the time required to investigate all injuries and attend to those of a more immediate danger. The investigators concluded that the idea that an ATAI should always take priority over other injuries was incorrect and they observed that the pharmacological reduction of wall stress appeared to decrease the probability of a rupture of the periaortic haematoma [13]. Despite the paramount importance of controlling blood pressure and cardiac contractility, the first multicentre trial of the *American Association for the Surgery of Trauma* ($AATS_1$) [25] revealed that only 17% of the 274 ATAI patients enrolled in that study had received correct treatment with beta-blockers. More recent studies reported a clear generalization of the use of beta-blockers for blood pressure and cardiac contractility control in ATAI patients [16, 32].

2.7.2. Open surgical repair

The thoracic aorta is optimally approached through a posterolateral thoracotomy, with an incision in the fourth intercostal space. The incision should be large enough to expose the aorta from the left common carotid artery for proximal control to the distal descending thoracic aorta for arterial inflow cannulation when needed. Notching the fifth rib posteriorly may help with this exposure. Proximal and distal control is accomplished before dissecting near the injury. The distal descending aorta is exposed first because it is the least likely to precipitate a free rupture of the contained haematoma. Indeed, because the injury most often occurs just distal to the origin of the LSA, it is usually not possible to expose the aorta distally to the LSA without disrupting the contained haematoma surrounding the injury. The descending thoracic aorta is controlled distally immediately after the traumatic injury to avoid sacrificing the intercostal arteries. The aortic arch can be controlled by either clamping between the left common carotid artery and LSA or just distal to the LSA depending on the level of the ATAI. Finally, the aorta can be repaired by direct suturing or graft interposition.

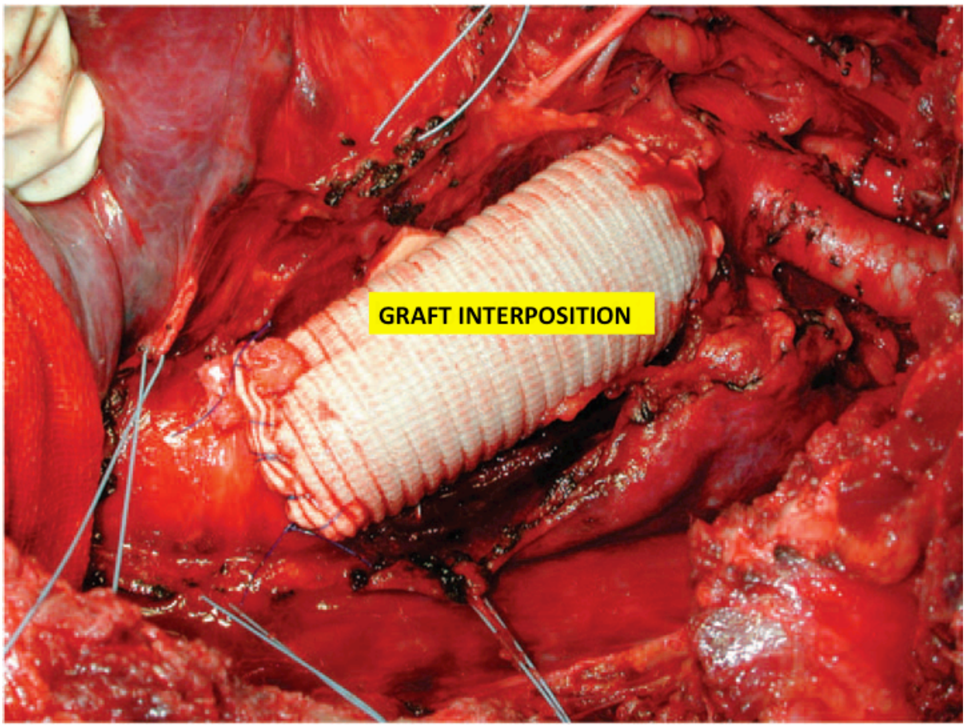


Figure 14. Repair of ATAI with Dacron graft interposition.

Open surgical repair can be performed with either simple aortic cross-clamping or with circulatory assistance (left heart bypass (LHB) with heparin-coated conduits, cardiopulmonary bypass (CPB) or femoral-femoral bypass). A significant controversy developed over whether there were differences in the results between simple clamp exclusion and direct repair (clamp and sew) and techniques that provide distal aortic perfusion during repair. Specifically, the most significant complication of thoracic aortic repair is paraplegia, the incidence of which seems to be reduced by the use of distal aortic perfusion techniques. We must bear in mind that, unlike patients with chronic aneurysmal disease, young trauma patients lack well-developed collateral circulation to the spinal cord and are therefore at increased risk of spinal cord ischaemia.

The open surgical repair of ATAIs has evolved significantly over time. In 1985, Svensson et al. [165] analysed literature reports of the operative mortality rate and incidence of paraplegia in 596 ATAI patients and compared total or partial cardiopulmonary bypass, passive perfusion shunts and simple cross-clamping. The mortality rates for the three procedures mentioned above were 16.7%, 11.4% and 5.8%, respectively. The mortality rate was significantly increased when distal perfusion techniques were used ($P<0.01$). However, the incidence of paraplegia among patients who underwent LHB, temporary shunting and simple aortic cross-clamping was 2.2%, 2.3% and 5.8% respectively ($P>0.05$). The investigators concluded that simple aortic cross-clamping was the method of choice in uncomplicated cases of ATAI. Nevertheless, a subsequent meta-analysis conducted by von Opell et al. [166] reviewed 1,742 patients and found that the risk of death was 18.2% with CPB, 11.9% for distal perfusion with LHB, 12.3% for shunts, and 16% for the "clamp and sew" method. The rates of paraplegia were 2.4%, 1.7%, 11.1% and 19.2%, respectively [166]. A comparable protective effect of distal aortic perfusion was demonstrated in a more recent cohort study and a systematic review by Jahromi et al. [167], and in a single institution study by Katz et al. [168].

Repair technique	Mortality rate	Paraplegia rate
Simple aortic cross-clamping	16%	19%
Passive shunts	12%	11%
Left heart bypass	18% (systemic heparinization) 12% (no systemic heparinization. Use of heparin-coated circuits)	2%

Table 7. Mortality and risk of paraplegia with ATAI repair procedures. (*) Data from von Opell et al. [166]

Of the many variables influencing the end result of operative repair of ATAIs, one of the most important might be the surgeon. This was clearly demonstrated by Albrink et al. [169], who found that better results were obtained when ATAIs were managed by experienced hands. This issue has been supported by other authors as well [170].

In conclusion, the open repair of ATAIs can be accomplished via different techniques according to whether or not an adjuvant distal perfusion method is used, presenting each technique different advantages/disadvantages that must be weighed up by the surgeon, as described in the following.

2.7.2.1. Simple cross-clamping technique

The simple cross-clamping technique, also called the “clamp and sew” technique, was the first described for the repair of ATAIs in the early fifties [171, 172]. The advantages of the simple cross-clamping technique are its simplicity and the lack of a need for heparin. In particular, this technique may be useful to the general, vascular or trauma surgeon who is not experienced in the utilization of extracorporeal perfusion circuits or the cannulation of cardiac chambers or great vessels when thoracic surgical expertise is unavailable. It may also be useful in unstable patients who are actively bleeding from an aortic tear; in these patients there may be no time to employ a distal aortic perfusion system.

Hilgenberg et al. [173] reported that the simple cross-clamping technique was associated with a relatively low risk of paraplegia (5.2%), and that the incidence of paraplegia was directly associated with the duration of cross-clamping and not with the use of passive shunts. Hunt et al. [174] reviewed the operative results of 86 patients with

ATAIs and found that no patient with a cross-clamping time of less than 35 minutes developed paraplegia. Nevertheless, 42.9% of the patients with longer cross-clamping times who underwent a "clamp and sew" repair method developed paraplegia. Other authors also emphasized the fact that low rates of paraplegia were achieved when aortic cross-clamping times were less than 25 to 30 minutes [25, 31, 175]. Recently, Bhaskar et al. [176] published their 20 years of experience with the clamp-and-sew technique for ATAIs with neither paraplegia nor 30-day mortality.

However, in the aforementioned meta-analysis von Opell et al. [166] highlighted the fact that the average cross-clamping time reported in the published literature was 41 minutes. Indeed, many cases of ATAI require more than 30 minutes to repair because of the amount of blood in the field, the fragility of the aorta and difficulties in identifying the local anatomy within a large haematoma. This is especially true if the tear extends proximally to involve the orifice of the LSA. These patients require clamping of the aorta proximal to the LSA, which may increase the incidence of paraplegia in the absence of distal aortic perfusion. Therefore, simple aortic cross-clamping should be reserved for patients in whom the anticipated clamping time is less than 20 to 25 minutes and for patients with a life-threatening haemorrhage [166, 168, 175].

The key to performing a successful simple aortic cross-clamping technique includes rapid exposure of the proximal aorta with minimal dissection of the injured area and minimal interruption of the intercostal arteries, and maximizing measures to avoid fluctuations in blood pressure, especially during clamping and declamping of the aorta. Effective pharmacological and blood volume management can achieve this objective.

2.7.2.2. Passive perfusion shunts

In the late fifties, increasing concern about catastrophic complications, mainly paraplegia, led to the use of proximal to distal aorta either biological or artificial shunts in order to provide some blood flow to the distal aorta during aortic cross-clamping [8, 177, 178].

One of the most frequently used passive perfusion shunts in thoracic aorta surgery is a tridodecylmethylammonium chloride (TDMAC)-heparin-coated shunt, named the Gott shunt, which was first described in 1963 by Gott et al. [179]. This TDMAC-heparin-coated shunt usually has one end placed in the aorta proximal to the proximal cross-clamp and one distal end located in the aorta distal to the distal clamp. Less commonly, the proximal end of the shunt may be placed in the left atrium or the apex of the left ventricle. The shunts are usually at least 9 mm in diameter and 90 mm in length because the flow is dependent on the diameter of the shunt and the pressure differential between the proximal and distal ends of the shunt. Besides providing distal flow, this shunt provides afterload reduction to the left side of the heart. The flow is usually greater than 2 l/min in 85% of patients [180, 181].

Stavens et al. [182] found that the incidence of paraplegia was significantly reduced by both extracorporeal circulation and the heparin-bonded Gott shunt; however, the former method was associated with a high incidence of postoperative bleeding in conjunction with systemic heparinization, and this, in turn, contributed to a high mortality rate. The investigators concluded that the Gott shunt provided the best protection, particularly in the setting of a training programme where a relatively small number of these operations are performed and cross-clamping times may be prolonged

[182]. Other authors [183-185] also highlighted the effectiveness of the Gott shunt in preserving the functional integrity of the spinal cord during cross-clamping of the thoracic aorta.

The placement of passive perfusion shunts requires a more extensive dissection of either the aortic arch or the ascending aorta. There may be difficulties inserting the shunt because of the position of the patient, periaortic haematoma or time constraints dictated by an expanding pulsatile and uncontrolled haematoma. There have also been anecdotal reports that brain-injured patients with an aortic injury repaired using these devices tend to get worse neurologically [25]. Furthermore, passive shunts do not offer the left ventricular unloading or loading advantage that partial bypass systems allow, and therefore blood pressure control is left to pharmacology alone [176].

Many authors have reported cross-clamping time to be the major risk factor associated with the development of paraplegia after the clamp-and-sew technique, and they have also emphasized the fact that there is no advantage in using passive perfusion shunts [25, 31, 175, 186].

2.7.2.3. Partial left heart bypass

In the partial LHB method, a small single- or dual-stage cannula is placed into the left atrium through the left inferior pulmonary vein to provide inflow to the pump. Outflow arterial cannulation can be performed by placing a high-flow aortic cannula in the distal descending aorta or, less commonly, a femoral arterial cannula. Femoral aortic cannulation has the advantage of convenience and speed. Partial LHB presents several advantages, namely, unloading the left heart and controlling proximal hypertension at the time of cross-clamping, maintaining lower body perfusion, allowing the rapid infusion of volume and controlling intravascular volume. The lower body is perfused at a flow rate of 2 to 3 l/min with a lower body mean arterial pressure of 60 to 70 mm Hg while maintaining an upper body mean arterial pressure of 70 to 80 mm Hg. All field blood is returned to the circuit via a pump reservoir or is accumulated and returned via cell saver. Ventricular arrhythmias pose a major risk since the native heart perfuses the upper body.

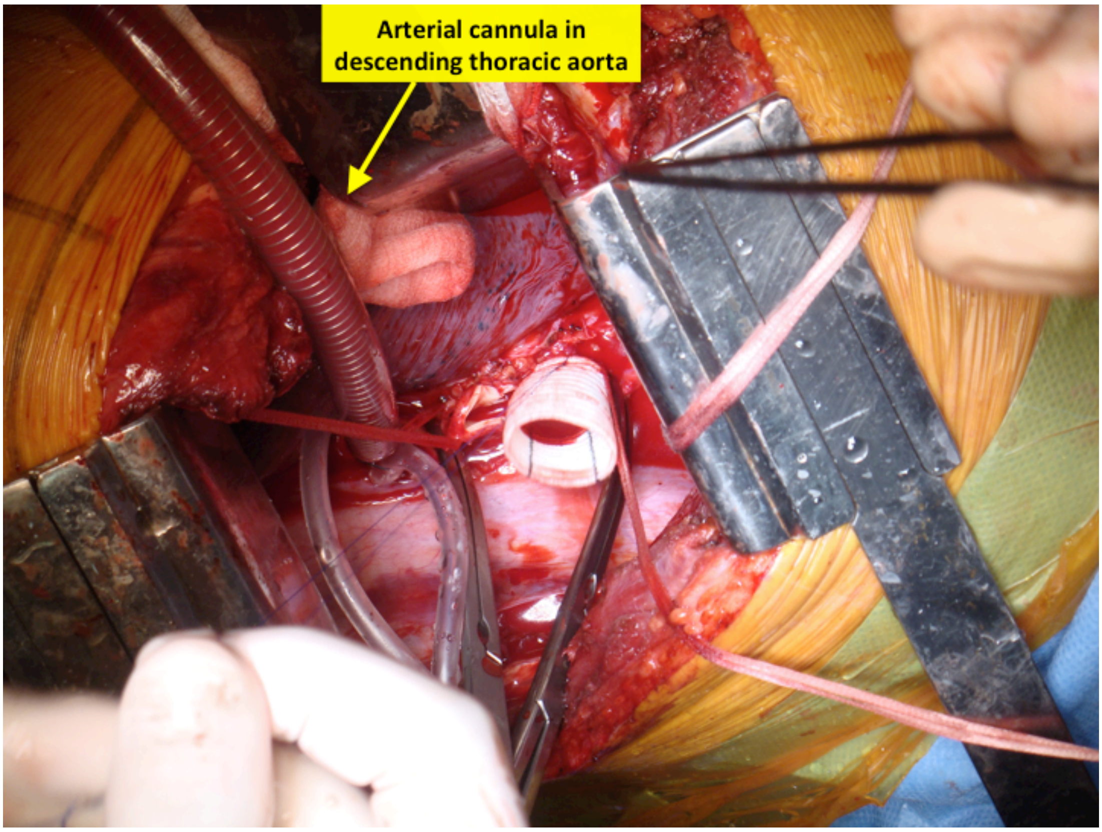


Figure 15. ATAI repaired using LHB. Notice the aortic cannula (arrow) placed in the descending aorta distal to the aortic injury for lower body perfusion.

Potential advantages of the LHB technique are that the distal aorta is perfused, which may help decrease rates of paraplegia as well as reduce ischaemia and reperfusion injuries associated with the sacrifice of hepatic, renal and mesenteric flow during simple aortic cross-clamping [25, 31, 175, 186].

In contrast, the disadvantages of both LHB and CPB are the need for systemic heparinization, which may predispose toward bleeding complications in patients with multiple injuries [176, 182]. The use of centrifugal pumps provides the advantages of distal perfusion while eliminating the potential hazards of heparin [187].

The results of a logistic regression analysis in a previously mentioned study by Hunt et al. [174] showed that not only was the cross-clamping time predictive of spinal cord injury, but the use of LHB was also independently predictive of protection against spinal cord injury. A review of the use of LHB with a heparinless centrifugal pump found that there was no instance of paraplegia [188]. Moreover, a comparison of the two multicentre trials of the *American Association for the Surgery of Trauma* ($AATS_1$ and $AATS_2$) revealed a significant increase in the use of the bypass technique in open repairs, from 64.7% in 1997 ($AATS_1$) to 83.8% in 2007 ($AATS_2$) [78].

2.7.2.4. Full or partial cardiopulmonary bypass

The use of total or partial CPB involves either direct right atrial cannulation at the inferior vena cava-right atrial junction from a left thoracotomy or venous cannulation through a long venous catheter with multiple side holes via the left common femoral vein into the right atrium. In some cases a right atrial-femoral arterial bypass was used with or without an oxygenator, such as a partial LHB. When no oxygenator is used, blood is returned with a partial arterial oxygen pressure of approximately 40 mm Hg (saturation 45 to 65%) so long as the haemoglobin concentration is maintained above 10 g/dl [189, 190]. Nonetheless, total CPB support is most useful in cases where the aortic arch is involved in the injury, in order to allow systemic cooling [191, 192]. Besides this, a total CPB may be preferred when there is concomitant right lung contusion in order to ensure adequate tissue oxygenation during repair.

Mattox et al. [193] reported mortality rates for the CPB, clamp-and-sew and shunt methods of 32.6%, 13.3% and 15.1%, respectively, and paraplegia rates of 4.5%, 8.3% and 10.3%, respectively. The significantly higher operative mortality rate was classically associated with systemic heparinization, which may increase rates of morbidity and mortality in patients with multisystem injuries (especially lung and brain injuries).

In the first multicentre trial of the *American Association for the Surgery of Trauma* ($AATS_1$) [25], the rate of paraplegia was lowest (2.9%) in 69 cases with the LHB centrifugal pump compared to partial or total CPB (6.6%) in 61 cases ($p>0.05$). Even though no significant complications were noted with heparin in the partial or total CPB groups and no differences were observed in the mortality rate compared to the centrifugal pump group, the LHB centrifugal pump eliminated the requirement for heparin [25].

More recently, Miller et al. [194] compared the operative outcomes of 28 ATAI patients who were operated on with CPB to those of 32 ATAI patients who were operated on without CPB. No patient in the CPB group developed paraplegia, whereas paraplegia occurred in 12% of the simple aortic cross-clamping group. Moreover, no patient in the bypass group experienced complications related to heparinization, but 7% presented bypass-related complications (cerebral oedema, femoral vein laceration) [194].

Very occasionally there may be a need to perform a proximal anastomosis under deep hypothermic circulatory arrest (DHCA) because an injury involves the mid-aortic arch [192]. Use of DHCA in trauma patients should proceed with caution and only after other serious associated injuries have been addressed in order to avoid bleeding complications. In cases of aortic arch transection close to the innominate or left common carotid artery, anterior exposure via sternotomy or thoracosternotomy may offer better exposure for total arch replacement [191, 192].

2.7.2.5. Additional measures for avoiding spinal cord ischaemia

In addition to lower body perfusion, several adjunctive measures can be used to reduce the risk of spinal cord ischaemia (SCI) during thoracic aortic surgery, such as monitoring motor or somatosensory-evoked potentials, lumbar cerebrospinal fluid (CSF) drainage and hypothermia [195-197]. Nonetheless, these modalities are often impractical in emergent settings. A large number of pharmacological agents have been evaluated for their neuroprotective effects in experimental studies of SCI, such as steroids, lidocaine or magnesium [198-200]. Thiopental and methylprednisolone have a wide clinical use for the protection of the brain and spinal cord during operations that require circulatory arrest and clamping of the descending aorta [201, 202]. These adjuncts have not been well studied in the trauma population and may not be feasible in most of multisystem trauma patients with critical associated injuries.

2.7.3. Endovascular repair

Designed to treat degenerative aneurysms of the thoracic and abdominal aorta, endovascular stent grafts have been increasingly employed as off-label emergency treatment for ATAIs. The thoracic endovascular approach for the repair of ATAIs was pioneered by Kato et al. in 1997 [203]. This technique seems to confer advantages in perioperative mortality and morbidity over traditional open surgical repair [15, 33, 204-206]. Nevertheless, TEVAR has not been prospectively studied for ATAI treatment; US Food and Drug Administration-approved devices are being used “off label” with considerable success based on retrospective studies. In a systematic literature review, Lettinga-van de Poll et al. [207] identified 284 ATAI patients who underwent TEVAR. The authors reported mortality rates ranging from 0% to 6%, whereas the procedure-related mortality rate was about 1.5%. A total of 6.7% of all of the procedures were complicated by an endoleak, and the overall procedure-related morbidity rate was 14.4% [207].

In a retrospective single-centre study conducted by Neschis et al. [208] on 20 ATAI patients treated by TEVAR, no procedure-related deaths were reported. Nine (45%) aortas were small enough to require the use of 23-mm abdominal cuffs, and six (30%) out of twenty cases required complete or partial coverage of the LSA. One patient presented a type I endoleak, whereas another patient suffered an endograft collapse [208].

In a study published by Tehrani et al. [205] on 30 patients with ATAI treated by TEVAR, the authors reported that technical success was achieved in 100% of the patients, as shown by angiographic and CT scanning. Three patients had complications: one iliac artery rupture, one cerebellar stroke and one partial stent collapse. There were two perioperative deaths and no instances of procedure-related paralysis.

In 2011, the *Society for Vascular Surgery Outcomes Committee*, including ad hoc members from the *Society of Thoracic Surgeons*, *American Association of Thoracic Surgery*, and the *Society for Interventional Radiology*, collected outcomes of patients with traumatic thoracic aortic transections treated with endovascular grafts [206]. The study enrolled 60 symptomatic patients with ATAIs and found an all-cause mortality rate of 9.1% at 30 days and 14.4% at 1 year. Major adverse events occurred early on in 20% and late in 3.6% of the patients. Death accounted for 41.7% of the early and all of the late major adverse events. The other early adverse events included 16.7% pulmonary, 13.3% neurological and 11.7% vascular complications. Late adverse events included one patient (1.8%) with pulmonary failure and one patient (1.8%) who died of an unknown cause. The investigators concluded that the 1-year results of endograft placement for the management of patients with ATAI (cumulative 1-year survival of 85.6%±5.2%) were acceptable, with approximately three-quarters of the deaths occurring in the first 30 days due to the acute severity of the trauma.

In almost all cases, aortic access in TEVAR for ATAIs is retrograde through the femoral or iliac arteries. As we have previously reported [209], TEVAR is performed in the operating room under general anaesthesia. Cardiopulmonary bypass is normally available on a standby basis during each stent placement procedure. A team of two cardiovascular surgeons and two interventional radiologists works together at our institution for TEVAR, and all procedures are monitored using a portable radiographic C-arm system Philips BV Pulsera™ (Philips Medical Systems, Best, The Netherlands) with digital subtraction angiography (DSA) [209].

Bilateral access is often obtained for angiography and delivery of the endograft. Percutaneous femoral, direct femoral and iliac arterial puncture and iliac access via a side Dacron graft sewn onto the iliac artery have all been used [67, 210]. After establishing arterial access, 5,000 units of heparin are routinely given intravenously [209], although it is possible to avoid heparin altogether in cases where there is concern for bleeding complications at remote sites [205]. A floppy J-tipped wire is advanced to the ascending aorta under fluoroscopic and/or TEE guidance. A marked catheter is subsequently passed over the wire. An aortogram is performed using a steep anterior oblique projection (~60º) in order to accurately assess and measure the aortic arch anatomy relative to the site of transection.

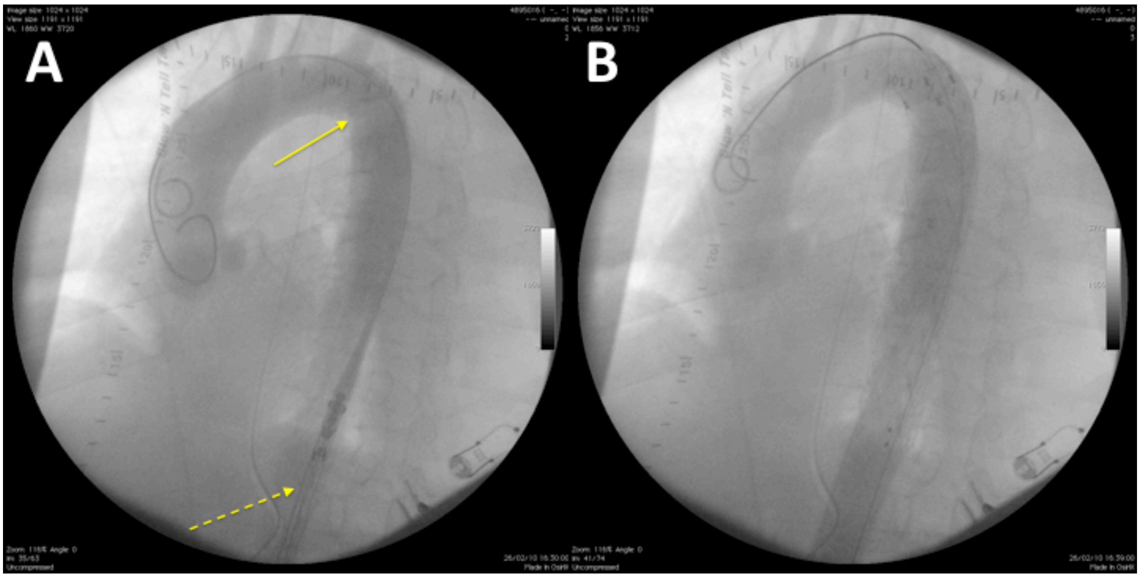


Figure 16. Intraoperative aortography (I). A. Intraoperative aortography performed using an anterior oblique projection of ~60º, showing a focal dissection at the level of the aortic isthmus (solid arrow) and the aortic endograft (dashed arrow) before deployment. **B.** Control aortography after endograft deployment, showing correct exclusion of the injured aorta.

Computed tomography images are routinely used to calculate stent graft dimensions, which are oversized by 10-15% compared to the landing zone diameters. The stent graft length is usually 30-40 mm longer than the target lesions, at least, in order to ensure adequate wall contact and a tight circumferential seal in the landing zones. A stiff wire is advanced from the side of device delivery. The device delivery sheath is advanced over the stiff wire under continuous fluoroscopy and the device is brought into position. The image intensifier is rotated to the ideal angle to completely visualize the aortic arch, and angiography is performed with breathing suspended [209]. The targeted landing zone can be marked on the fluoroscopy screen with a felt pen or a roadmap programme can be used when available. The pigtail catheter used for the angiogram is subsequently withdrawn and the stent graft is deployed under fluoroscopy.

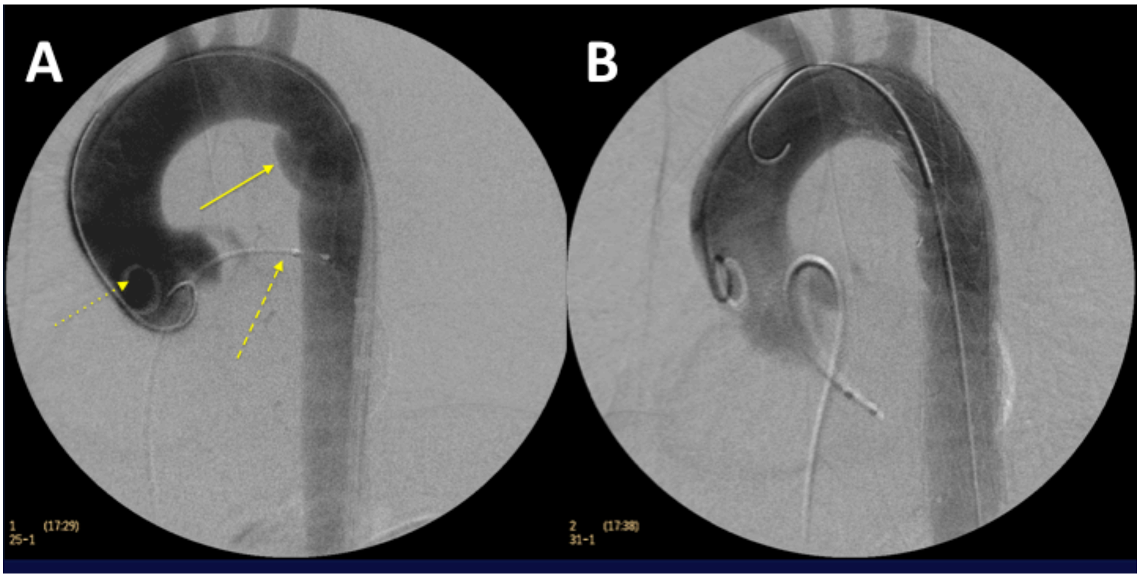


Figure 17. Intraoperative aortography (II). A. Intraoperative aortography confirmed a complete aortic transection (solid arrow) in a young male after an MVC. Notice the diagnostic pigtail at the aortic root (dotted arrow), coming from the right common femoral artery, and a temporary transvenous pacing catheter (dashed arrow) inserted through the right femoral vein. **B.** Control aortography after endograft deployment shows correct exclusion of the injured aorta.

Follow-up is usually based on guidelines for evaluating thoracic endografting for atherosclerotic aneurysms with CT angiography performed during the first postoperative week, at the time of discharge, and at 1, 6 and 12 months [15, 81, 163, 211].

The *Expert Opinion Committee of the Society of Thoracic Surgeons* [211], the *Clinical Practice Guidelines of the Society for Vascular Surgery* [81], the *American Association of Thoracic Surgeons* [15], and the *ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease* [163] suggest that endografts might be considered for the treatment of ATAIs. Nevertheless, some measures of caution must be taken because of the possibility of device and procedure-related complications, especially in young patients, and the lack of information regarding the long-term durability of endografts [15, 81, 163, 211].

The types of complication that can occur after TEVAR include endoleak, stent-graft collapse, stroke, embolization, bronchial obstruction, migration, paralysis, dissection and rupture [67]. One of the most frequent problems with endovascular grafting for ATAIs is the need to cover the LSA, but an associated LSA revascularization is rarely required, unlike in other non-ATAI TEVAR procedures [212]. In TEVAR for ATAIs, endografts are usually placed in the distal arch or proximal descending aorta, or both, and they are relatively short compared to what is commonly required to bridge more extensive degenerative aneurysms [213-215]. Hence, the coverage of intercostal arteries is very limited, especially between the T6 and L1 vertebral levels. In cases of ATAI, the deployment of short endografts (usually of <150 mm) in the proximal descending aorta most likely influences the risk of paraplegia and may account for lower procedural rates of spinal cord ischaemic events in relation to those associated with the open repair of transections and TEVAR treatment for more extensive non-traumatic lesions.

On the other hand, device oversizing by more than 20% is contraindicated because the endograft can fold in on itself and obstruct the aorta. This may also lead to detrimental increased radial force on the aorta. In addition, because most patients are quite young, the aorta has generally not become enlarged and unfolded; thus, the acute angulation of the arch can be difficult to accommodate. If the proximal end of the stent graft is not apposed to the aortic wall on the lesser curve of the arch ("bird beak deformity"), the graft can become compressed by the pulse pressure under the proximal lip of the stent graft, resulting in a proximal type I endoleak. Indeed, the use of oversized devices in small aortas and imperfect proximal apposition to the lesser curvature carry a risk of device failure by collapse, which may have life-threatening clinical repercussions [216-218]. When clinically indicated, percutaneous repair can be effectively performed by bare stenting [218]. In a review of six cases of endograft collapse or infolding with the TAG system (W. L. Gore & Associates, Flagstaff, Ariz), the authors [219] highlighted the fact that the endoprosthesis collapse occurred in patients who had a smaller aortic diameter than recommended by the manufacturers for the use of these prosthesis. The investigators emphasized the fact that caution should be exercised when contemplating TEVAR in patients with an aortic diameter of <23 mm [219].

A more recent review of TEVAR in ATAI by Atkins et al. [220] raised concerns regarding the use of aortic endografts in patients <18 years of age because most of these patients have small aortas, and the current generation of devices would be grossly oversized. Moreover, little information is available regarding the long-term consequences of placing an endograft in a young person who has not yet reached full maturity, as well as the effects of cumulative radiation exposure from multiple CT scans. Likewise, TEVAR should be avoided in patients with an outer wall aortic diameter <18 mm in order to prevent dangerous oversizing [220].

Stroke occurs at a rate of 3% to 5% in thoracic endografting, although the incidence is reported to be lower in the trauma population, at 0% to 2% [221]. Possible causes may include occlusion of the left vertebral artery, embolization of arch thrombus in older patients, inadvertent guidewire advancement into the carotid artery or air embolism.

2.7.3.1. *LSA management during zone 2 coverage*

As we have reported in previous chapters, published clinical series have shown that ATAIs occur at the isthmus in 54.7% to 74.5% of cases [15, 25, 32, 76-78], which may require covering of the LSA (zone 2 [222], Figure 18) in order to achieve a suitable proximal landing zone (length >1.5 cm) for safe endograft deployment.

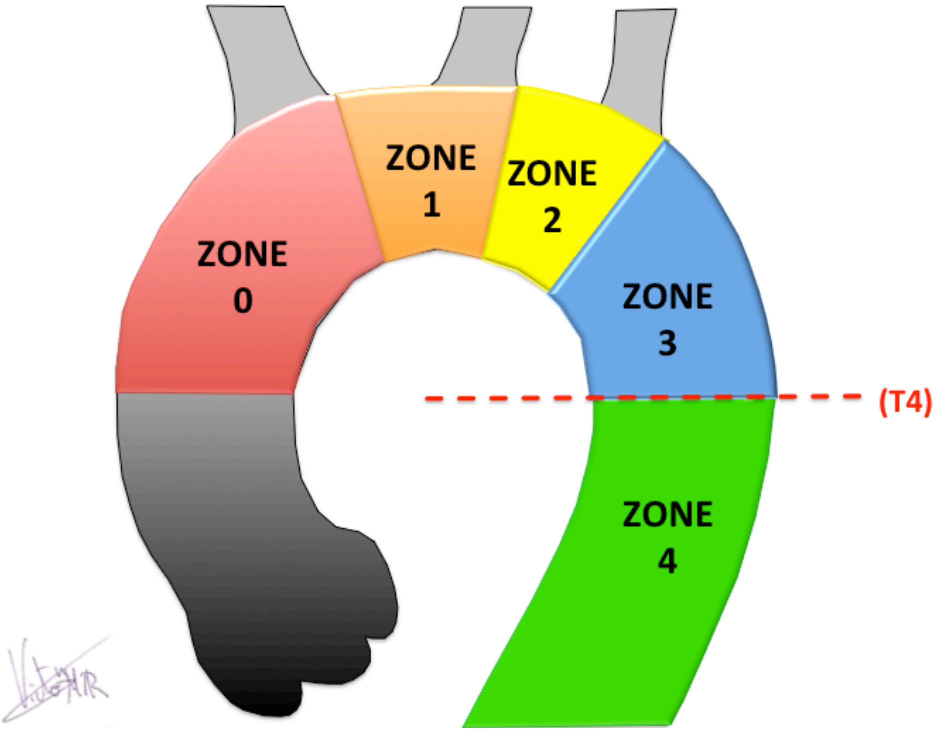


Figure 18. Classification of proximal landing zones for endograft deployment [222].

In a systematic review by Dunning et al. [223] about the safety of covering the LSA when stenting the thoracic aorta, the authors found 498 cases where the LSA was covered during TEVAR in 20 published studies. The types of complication reported after LSA coverage included strokes in 2.6%, paraplegia or paraparesis in 1.6% and endoleaks in 1.2% due to subclavian backflow. In addition, 10% of cases had ischaemia or other symptoms attributable to poor blood flow, which resulted in post-procedural revascularizations in 4%. The investigators concluded that coverage of the LSA has a low, but not insignificant, incidence of side-effects. Therefore, the risk of these potential complications must be balanced with the urgency of the procedure and may be only acceptable in emergency or salvage situations. However, in non-emergency cases the carotid arteries, the vertebral arteries and the Circle of Willis must be fully assessed by tests such as duplex ultrasound, angiography, CT or MRI scanning. An absent right vertebral artery, diseased carotid arteries or an incomplete Circle of Willis is a contraindication to LSA coverage without prior transposition or bypass grafting of the LSA.

On the other hand, some authors [224] recommended that in the presence of an inadequate proximal landing zone, conventional open surgical repair still remains a favourable option as an alternative to endovascular procedures if surgical revascularization of the LSA, carotid artery or both is necessary.

Kotelis et al. [225] found that the indications for revascularization of the LSA when performing TEVAR include coverage of a long segment of the aorta, prior or concomitant infrarenal aortic replacement and renal insufficiency. In addition, a hypoplastic right vertebral artery, a patent left internal mammary artery graft and a functioning dialysis fistula in the left arm are also indications for performing revascularization. Similarly, in 2009, the *Society for Vascular Surgery* published the

Practice Guidelines: Management of the left subclavian artery with thoracic endovascular aortic repair [226]. The committee issued three recommendations:

I. In patients who need elective TEVAR where the achievement of a proximal seal necessitates coverage of the left subclavian artery, routine preoperative revascularization is recommended, despite very low-quality evidence (GRADE 2, level C).

II. In selected patients who have an anatomy that compromises perfusion to critical organs, routine preoperative LSA revascularization is strongly recommended, despite very low-quality evidence (GRADE 1, level C).

III. In patients who need urgent TEVAR for life-threatening acute aortic syndromes where the achievement of a proximal seal necessitates coverage of the LSA, revascularization should be individualized and addressed expectantly on the basis of anatomy, urgency and the availability of surgical expertise.

Consequently, the current clinical practice guidelines of the *Society for Vascular Surgery* [81] for the endovascular repair of ATAIs recommend that LSA revascularization must be individualized depending on the status of the vertebral anatomy.

2.7.3.2. Spinal drainage

As spinal cord perfusion pressure is determined by the gradient between mean arterial pressure (MAP) and CSF pressure, the cornerstones of management for SCI during TEVAR are maintaining a MAP of >90 mmHg and a CSF pressure of 10 cm H_2O [227, 228]. However, no data exist regarding the use of prophylactic spinal drainage for traumatic injuries. Several risk factors have been identified as being related to SCI after

TEVAR. It was found that the length of aortic coverage was an independent predictive factor of SCI with 205 mm as a threshold for increased risk [229, 230]. Other independent factors associated with a higher incidence of paraplegia are the use of three or more stent-grafts and LSA coverage without revascularization [231-233], as well as simultaneous or previous open infrarenal aortic replacement [234]. Nonetheless, SCI is a low-incidence event, ranging from 0.8% to 1.8% after TEVAR for traumatic injuries [15, 235].

On the other hand, potential CSF drainage-related complications must not be neglected, such as bloody spinal fluid (5%), epidural haematoma (2.9%) and even mortality (0.9%) [236, 237].

In summary, based on the proximal location of the injury, limited coverage of the thoracic aorta and the risk of epidural haematoma in a coagulopathic patient, routine use of spinal drainage is not recommended by current clinical practice guidelines for TEVAR in ATAI, and it should only be used for symptoms of SCI [81].

2.7.4. Open repair versus endovascular repair

For many decades open surgical repair has been the traditional method of treating ATAIs. However, in the last few years the advent of TEVAR for the treatment of thoracic aorta pathologies has led to a shift towards endovascular management of patients with ATAIs. Thoracic endovascular aortic repair allows rapid exclusion of the aortic lesion and is less invasive than open surgery, which is particularly desirable in patients with ATAI and multiple associated injuries. It also appears to reduce mortality and morbidity rates in patients with ATAIs [15, 238-241]. Moreover, TEVAR has extended operative treatment to patients who were not previously considered suitable candidates for repair [235], as it allows the prompt exclusion of the aortic injury and does not require thoracotomy or aortic clamping, which are undesirable in unstable patients with multiple associated injuries. Blood loss is reduced and systemic heparinization and perioperative single lung ventilation are required less often. Therefore, pulmonary complications are significantly reduced with TEVAR. An increased incidence of pneumonia after open repair of ATAIs compared to TEVAR has been described by some authors [15, 239]. Likewise, paraplegia, which is probably the most devastating complication of thoracic aortic interventions, occurs in approximately 5.6% to 7% of patients after open surgery compared to less than 1% after TEVAR [34, 235, 241-243].

Due to the relative infrequency of hospital admissions with ATAIs, most studies to date have been single-institution retrospective reports. However, there are several systematic reviews and meta-analyses comparing the published literature on open repair versus TEVAR in ATAI treatment [34, 235, 240-243]. One must always take into account the phenomenon of publication bias when considering such data, as negative results are possibly never published. In fact, the only large evaluation that did not support the superiority of TEVAR for ATAI was a study conducted by Arthurs et al. [26], which identified 3,114 patients with ATAIs among 1.1 million trauma admissions between 2000 and 2005 from the *US National Trauma Data Bank*. The authors did not find any statistically significant differences in 30-day mortality between open repair (665 patients) and TEVAR (95 patients) (19% vs. 18%, $P>0.05$). Binary logistic regression showed that aortic repair, regardless of the technique used, was the only variable associated with improved survival (OR = 0.36; 95% CI: 0.24-0.54, $P<0.05$) when controlling for the physiological presentation and associated injuries. Interestingly, endovascular repair was not associated with an advantage in survival over open repair. Nonetheless, the endovascular devices used in the period evaluated (2000-2005) were custom-made devices or the off-label use of aortic cuffs [26]. This may explain the negligible improvement found in the mortality rate after TEVAR in their analysis compared with other studies published in the literature. The authors also reported that open repair was associated with higher cardiopulmonary complications (acute respiratory distress syndrome, pneumonia and myocardial infarctions), whereas endovascular repair was associated with higher rates of acute renal failure [26].

Tang et al. [243] analysed 33 articles reporting on 699 patients, where 370 were treated with TEVAR and 329 with open surgery. No differences were found in age, injury severity score (ISS) or technical success rates. The mortality rate was significantly lower for TEVAR (7.6% versus 15.2%, P=0.008), as were the rates of paraplegia (0% versus 5.6%, P=0.001) and stroke (0.85% versus 5.3%, P=0.003). TEVAR-associated complications were not specifically analysed, and long-term results were not available. In another meta-analysis on this topic, Xenos et al. [34] found similar results with a lower postoperative mortality rate (OR 0.44, P=0.005) and ischaemic spinal cord complications (OR 0.32, P=0.037) for TEVAR compared to open surgical repair.

In 2010, Jonker et al. [241] reviewed all cases of ATAIs in New York State between 2000 and 2007, which comprised a total of 328 patients, of whom 79.6% underwent open repair and 20.4% TEVAR. After controlling for significant covariates, TEVAR independently reduced the risk of death following surgical intervention for ATAI compared to open procedure (OR 3.8, 95% CI, 1.28-10.99; P=0.01). Respiratory complications were the most common postoperative morbidity and were significantly increased after open repair: 38% vs. 24% (OR 1.95; 95% CI, 1.05-3.60; P=0.032). The authors also found an incidence of 9% endoleaks and distal embolization in patients after TEVAR [241].

However, the only large prospective multicentre study was supported by the

American Association for the Surgery of Trauma to assess the early efficacy and safety of TEVAR for ATAI versus standard open repair in 2007 ($AAST_2$) [15]. In the 18 major US trauma centres included in the trial, the decision for open or endovascular repair was left to the surgeon's preference. The primary outcome measure was in-hospital mortality; the secondary endpoints included complication rates, ventilator days, transfusion requirements and ICU and hospital lengths of stay. A total of 193 patients met the inclusion criteria. Overall, 125 patients (64.9%) were selected for TEVAR and 68 (35.2%) for open repair. Thoracic endovascular aortic repair was selected for 71.6% of the 74 patients with major extrathoracic injuries and 60% of the 115 patients with no major extrathoracic injuries. The TEVAR patients were significantly older than the open repair patients. Overall, 25 patients in the TEVAR group (20%) developed 32 device-related complications. There were 18 endoleaks (14.4%), 6 of which needed open repair. The authors reported that procedure-related paraplegia developed in 2.9% of patients in the open repair group and 0.8% of patients in the TEVAR group ($p=0.28$). Multivariable analysis adjusting for severe extrathoracic injuries, hypotension, GCS and age showed that the TEVAR group had a significantly lower mortality rate and fewer blood transfusions than the open repair group. Among the 115 patients without major extrathoracic injuries, a higher mortality rate and greater transfusion requirements were also found in the open repair group. Among the 74 patients with major extrathoracic injuries, significantly higher rates of mortality and pneumonia were found in the open repair group. Multivariate analysis showed that centres with a high volume of endovascular procedures had significantly fewer systemic complications and shorter lengths of hospital stay than low-volume centres. The investigators found that most surgeons selected TEVAR for ATAIs, irrespective of associated injuries, injury severity or age. In addition, the $AAST_2$ group concluded that TEVAR is associated with a significantly lower rate of mortality and fewer blood transfusions, but that there is a considerable risk of serious device-related complications [15].

More recently, a study performed by Hong et al. [235] compared the evolution of ATAI treatment (non-operative, open repair and TEVAR) in the US from 2001 to 2007, dividing the cases into two time periods, before and after the widespread adoption of TEVAR (2001-2005 and 2006-2007). A comparison of the two time periods showed an increase in the number of TEVAR procedures with a simultaneous decrease in open repair in the period of 2006 to 2007. The TEVAR group contained a higher percentage of patients with brain injury (26.1% vs. 20.6%; P=0.008), lung injury (25.0% vs. 17.7%; $P < 0.001$) and hemothorax (32.5% vs. 21.7%; $P < 0.001$) than the open surgery group. No differences were found in the number of intra-abdominal injuries or major skeletal fractures. The open surgery group had more respiratory complications (43.9% vs. 54.2%; $P < 0.001$), whereas the TEVAR group had a higher rate of stroke (1.9% vs. 0.7%; P=0.021). The authors did not find differences in the rate of paraplegia or renal failure. The overall rate of in-hospital mortality was 23.2% (non-operative group 26.7%, open repair 12.4% and TEVAR 10.6%). Although the investigators did not find any significant differences in the rate of mortality between the open repair and TEVAR groups, Hong et al. [235] surmised that this lack of a statistically significant difference reflected the multisystem nature of injury and a greater preoperative risk in the TEVAR group. In addition, the authors concluded that the widespread use of TEVAR was associated with a decrease in the overall mortality rate from ATAIs.

Finally, it must be emphasized that TEVAR is still associated with a number of considerable complications, such as endoleak, graft fracture and graft migration, necessitating life-long surveillance [216-220]. Caution should be taken with the widespread use of TEVAR for ATAIs until more is known about the long-term behaviour of the devices, especially in young trauma patients.

2.7.5. Operative timing: early versus delayed repair

The classic autopsy and clinical study of Parmley et al. in the late fifties reported a death rate at the scene of as high as 85% and a subsequent mortality rate in non-operated survivors of 1% per hour for the first 48 hours [2]. Moreover, of the surviving patients, approximately 5% were haemodynamically unstable or deteriorated within 6 hours of admission, leading to an in-hospital mortality rate as high as 90% or more [29]. In the 1960s and 1970s, as trauma systems developed and the transportation of critically ill trauma patients improved, many people who would have previously died at the scene were now arriving at trauma centres in extremis. Most of these patients subsequently died during the early phase of care. These patients were included in the early studies of ATAIs and likely skewed the interpretation of the data to suggest that all patients with ATAIs were imminently unstable and required urgent repair. Nevertheless, since the 1990s, delayed surgical repair has been considered in patients with ATAIs who present with haemodynamic stability and who do not have imaging findings showing impending rupture [244]. The reason behind this trend is that in the majority of the patients who make it to the hospital alive, the adventitia and surrounding mediastinal structures remain partially intact, thus preserving the integrity of the disrupted aorta [245]. In addition, an increasing number of subsequent studies suggested that some select patients with major associated injuries could be safely managed with delayed repair, provided that blood pressure and contractility were adequately controlled [12, 246].

As we have mentioned in previous chapters, no two aortic injuries are the same or have a similar prognosis. Indeed, Karmy-Jones et al. [30] noted that there were three broad categories of patients who sustained an ATAI. The largest group (70% to 80%) comprised those who died at the scene. The second group is unstable upon presentation to hospital or become unstable shortly thereafter, and comprise just 2% to 5% of the patients with ATAIs. The final group (20% to 25%) remain haemodynamically stable after the aortic injury, and any mortality is secondary to associated injuries.

In the first multicentre prospective study conducted by the *American Association for the Surgery of Trauma* ($AAST_1$) [12], the patients were classified into four groups according to their clinical status, which determined their subsequent management: (1) in extremis: patients who presented with some vital signs and who underwent emergent thoracotomy; (2) stable: patients who underwent planned thoracotomy after diagnostic evaluation; (3) rupture: patients who were admitted with haemodynamic stability and developed aortic rupture before planned thoracotomy; (4) non-operative: patients who underwent a diagnostic evaluation but did not have a thoracotomy because of either associated injuries or advanced age.

Multiple studies have reported the safety of the delayed surgical repair of ATAIs in multisystem trauma patients by first addressing other life-threatening injuries [13, 16, 25, 247-249]. Furthermore, we recently showed that definitive non-operative management may be a therapeutic option with acceptable survival rates in carefully-selected patients with multiple severe associated injuries or high risk co-morbidities [36]. Nonetheless, the potential for the rapid progression of ATAIs in the same patients mandates serial radiological controls during the first 3 months after diagnosis and then annually thereafter [36].

One of the major contributions towards shedding light on the timing of aortic repair in ATAIs was the analysis of data provided by the second multicentre prospective trial conducted by the *American Association for the Surgery of Trauma* ($AAST_2$) [16]. A total of 178 patients with ATAI were eligible for inclusion and analysis, 109 (61.2%) of them underwent early repair and the remaining 69 (38.8%) patients delayed repair. The two groups had similar epidemiological, injury severity and repair type characteristics. The adjusted mortality rate was significantly higher in the early repair group, whereas the adjusted complication rate was similar between the two groups. However, delayed repair was associated with significantly longer lengths of stay in the ICU and hospital. The analysis of 108 patients without major associated injuries showed that there was a trend towards a higher mortality rate in early repair but a significantly lower complication rate and shorter ICU stay than in the delayed repair group. Likewise, the analysis of 68 patients with major associated injuries showed a strong trend towards a higher mortality rate in the early repair group. The rate of complications was similar between both groups. Therefore, the $AAST_2$ group concluded that the delayed repair of stable ATAIs is associated with improved survival irrespective of the presence or absence of major associated injuries. Nonetheless, the authors also highlighted the fact that delayed repair is associated with a longer length of ICU stay and, in the group of patients with no major associated injuries, a significantly higher rate of complications.

The current *Clinical Practice Guidelines of the Society for Vascular Surgery* [81] suggest urgent (<24 hours) repair, barring other serious concomitant non-aortic injuries, or repair immediately after other injuries have been treated, but at the latest prior to hospital discharge [81].

Some authors [16, 32, 247, 248, 250] suggested that the following factors should be considered for initial medical therapy followed by delayed repair (Table 8).

Recommended clinical factors for a delayed repair
1. Brain injury with significant haemorrhage or oedema on CT scan.
2. Pulmonary contusion with a PaO2/FiO2 ratio less than 300, positive end-expiratory pressure requirements of 7.5 cm H2O, or the inability to tolerate single-lung ventilation.
3. Pre-existing cardiac disease: recent angina, earlier coronary artery bypass surgery, requires inotropic support.
4. Coagulopathy: non-surgical bleeding, international normalized ratio greater than 1.5, platelets less than 40,000.
5. Intra-abdominal solid organ injury.
6. Severe pelvic fracture.

Table 8. Recommended clinical factors for a delayed repair [16, 32, 247, 248, 250]**.**

In contrast, the emergent repair of an ATAI should undoubtedly be considered when there is even a slight risk of impending rupture, namely, an enlarging aortic lesion, evidence of pseudocoarctation, and/or a large hemothorax [16, 32].

In summary, the correct timing of ATAI repair in a patient with mutisystem trauma should be considered and balanced along with the presence or absence of other severe injuries, without a fixed priority.

2.7.6. Definitive conservative management

Although the traditional approach for ATAIs is emergent (<24 hours) surgical repair, as we have previously mentioned the trend today is towards delayed repair (open or endovascular), since several studies have suggested that some patients with major associated injuries [246], or even with no severe associated injuries or major comorbidities [16], can safely be managed with delayed repair provided that blood pressure and contractility are adequately controlled.

It may be tempting to adopt a definitive non-operative management for patients in whom a haemodynamically stable situation is achieved with medical therapy, especially if major extrathoracic injuries are associated.

The anatomic structure of the aortic wall may explain the amenability of limited intimal injuries for conservative treatment. The aortic wall is composed of an internal layer, the intima, a middle layer, the media, and an outer layer, the adventitia. The media is composed of sheets of elastin interspersed with smooth muscle cells and provides most of the structural strength and elastic properties of the aorta. Therefore, injuries limited to the intimal layer should not compromise the resistance of the aortic wall and may be suitable candidates for non-operatively management provided that aortic wall stress and cardiac contractility is appropriately controlled with beta-blockers. Besides, animal studies support that aortic wall injuries limited to the intimal layer are successfully repaired by endothelization in nearly all the subjects [251].

Holmes et al. reported the results of a study of 30 patients with ATAIs divided into either a group treated with delayed surgery or a non-operatively managed group with a median follow-up of 2.5 years. In this report, one third of the patients from the non-operative group died within the first 5 days. Moreover, the non-operatively managed patients were significantly older and tended to be more severely injured according to the ISS score [249].

In 2002, Kepros et al. [252] reported a mini-series of 5 patients with conservative management after ATAI in whom the complete resolution of small intimal tears (<20 mm) was achieved by TEE between 3 and 19 days. After a review of non-operative series in the literature, the largest one including 19 patients, Hirose et al. [253] concluded that the non-operative management of ATAIs may be the treatment of choice in select patients, especially in those with multiple associated injuries or severe comorbidities and in those with an aortic flap < 10 mm.

Caffarelli et al. [254] recently published the early outcomes of 29 patients who underwent planned non-operative management with a survival rate of 97% at a median of 1.8 years (range, 0.9-7.2 years). This study concluded that the deliberate, non-operative management of carefully selected patients with traumatic blunt aortic injury may be a reasonable alternative for the multisystem trauma patient. However, the serial imaging and long-term outcome results (survival and aortic-related complications) remained obscure.

In a retrospective analysis of the *US National Trauma Data Bank* from the years 2000 to 2005, Arthurs et al. [26] identified 3,114 trauma patients with ATAIs among 1.1 million trauma admissions. A total of 68% (1,642 patients) were managed non-operatively, 28% (665) underwent open repair, and 4% (95) underwent endovascular repair with associated mortality rates of 65%, 19% and 18% respectively. The patients who were managed non-operatively presented a higher proportion of $GCS \leq 8$ on admission (66% vs. 24% and 21%, $P<0.05$) and a higher mean ISS (39 ± 16 vs. 36 ± 12 and 37 ± 14, $P<0.05$). Using binary logistic regression, the authors concluded that aortic repair, either open surgical or endovascular, was the only variable associated with improved survival rates (OR = 0.36; 95% CI: 0.24-0.54, $P<0.05$) when controlling for physiological presentation and associated injuries.

In 2011, Hong et al. [235] identified 8,269 trauma patients with ATAIs among the *US National Inpatient Sample Database* from the years 2001 to 2007. Although the authors did not report the precise number of patients who underwent conservative management and focused on both endovascular and open repair, the in-hospital mortality rate was higher in the non-operative group (26.7%) than in the open repair (12.4%) and TEVAR (10.6%) groups ($P=0.273$). The investigators also found that the non-operative mortality rate decreased from 28% to 23.2% ($P<0.001$) when the period 2001-2005 was compared with the period 2006-2007 [235].

We recently reported the largest single-centre series with the longest follow-up of definitively non-operatively managed ATAI patients to date [36]. It was a 30-year follow-up series that included 66 major trauma patients with ATAIs who were classified according to the type of definitive management chosen (open surgery, endovascular repair or non-operative management). Figure 19 shows the design of our aforementioned study [36].

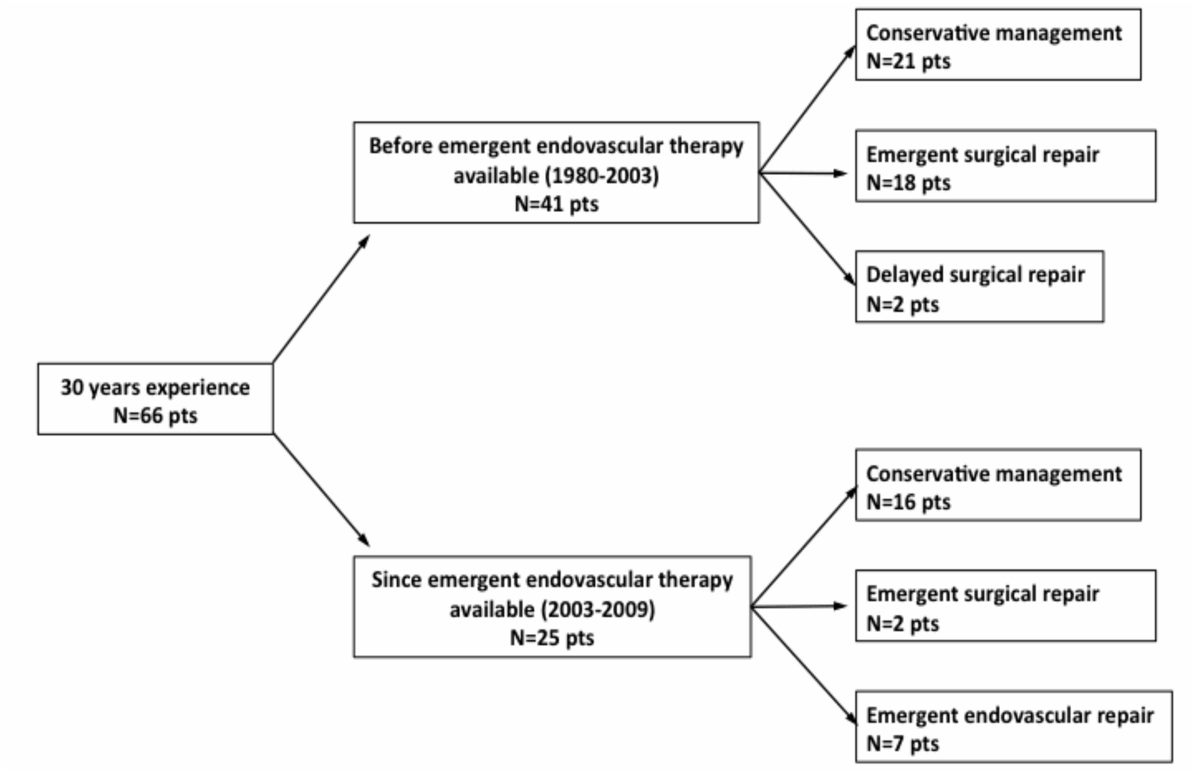


Figure 19. Modification in ATAIs management since incorporation of emergent TEVAR. This flowchart shows the modifications in patient management since the incorporation of emergent aortic endografting at our institution [36].

The non-operative group included patients who were not initially considered for surgical or endovascular intervention because of patient-family decisions in 6 patients; clinical judgements in 12 low-risk patients, including patients with an intramural haematoma without an intimal tear or an intimal flap <10 mm; and severe associated injuries, advanced age or other severe pre-morbid conditions in 19 high-risk patients. Two patients from the conservative group required emergent surgical or endovascular treatment because of in-hospital aortic-related complications during the first 15 days of hospitalization. The in-hospital mortality rate was similar between the three groups, but with a slightly lower in-hospital death rate in the endovascular group (14.3% endovascular vs. 21.6% conservative and 22.7% surgical groups, *P*=0.57). In contrast, the expected in-hospital mortality tended to be higher in the endovascular group according to the trauma scores, although this difference was not statistically significant. Indeed, all of the in-hospital aortic-related complications (free aortic rupture or progression of dissection) only occurred in the conservative group and led to either a switch to endovascular or surgical management or directly to patient death.

With a median follow-up of 75 months, our study [36] showed that patients who underwent non-surgical management had a greater long-term probability of developing aortic-related complications after discharge than those who were treated with surgical or endovascular management (37.9% vs. 0%, P=0.004). We found that the initial type of aortic lesion (HR: 2.94, P=0.002) and a TRISS score >50% (HR: 1.49, P=0.042) on admission were risk factors for a worse long-term prognosis [36]. Furthermore, we detected two peaks in the complication rate of the non-surgical group. The first peak occurred during the first week and mainly affected patients with a major or borderline aortic radiological injury. The second peak appeared between the first and third months after the blunt thoracic trauma. Indeed, two patients from the conservative group suffered a critical aortic-related complication (free aortic rupture) between the first and third months after thoracic trauma. Both presented with an aortic intimal tear > 10 mm [36].

The long-term survival rate tended to be poorer in the conservative group than in the surgical and endovascular groups (72.3% conservative compared with 78.2% surgical and 85.7% endovascular at 5 years, P=0.18) (Figure 20) [36]

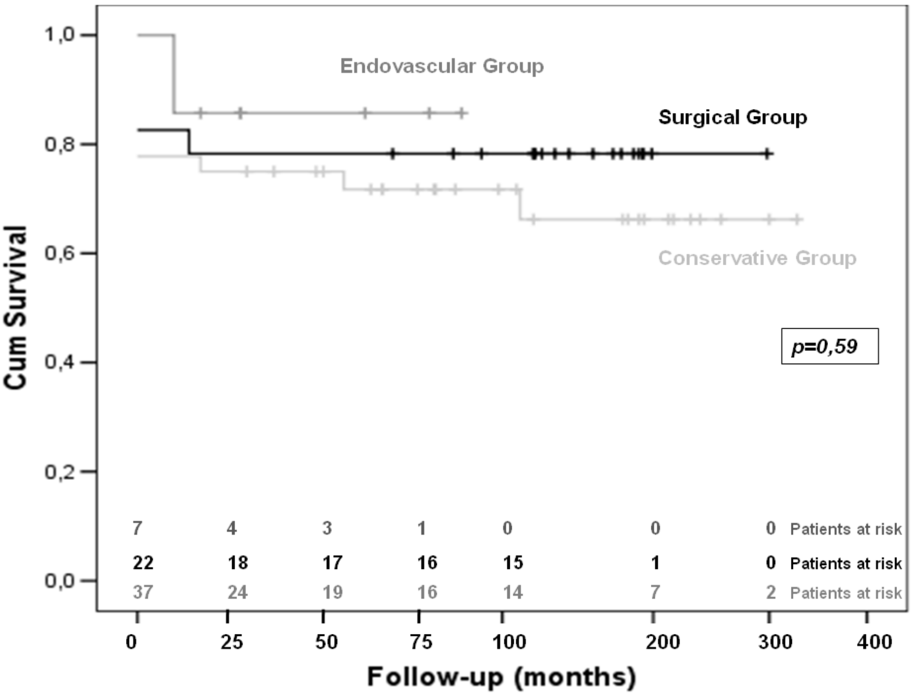


Figure 20. Kaplan-Meier survival curves of different strategies of management of ATAI patients. The Kaplan-Meier survival curves for the conservative, surgical and endovascular groups, including in-hospital mortality, show a clear trend towards greater long-term survival in the endovascular group, without being statistically significant (*P*=0.59) [36].

In 1995, Pate et al. [13] undertook a study to explore whether or not the surgical repair of ATAIs without signs of impending rupture could be safely delayed. The authors reviewed the medical records of 112 patients with ATAIs at the aortic isthmus. Fifty of these patients received medical treatment aimed at decreasing aortic wall stress. Eight patients died before aortic repair, six of aortic exsanguination (all within 4 hours of injury). Of the 77 patients for whom the time of injury was recorded and the aorta was repaired, 36 were repaired within 12 hours of injury and 41 between 12 hours and 24 weeks; none developed an aortic haemorrhage. No patient who received adequate medical therapy died of a rupture of the haematoma. Other major surgeries preceded aortic repair in 33 patients. Pate et al. [13] also reported that only 7% of the patients with a history of untreated ATAIs developed a chronic thoracic aortic aneurysm. In contrast to that results, our group found that the aortic injury progressed to a post-traumatic aneurysm in 8 (27.5%) out of the 29 patients of the conservative group who survived and were discharged from hospital [36]. In fact, all of these post-traumatic aneurysms required late surgical or endovascular repair of the aneurysm during the follow-up period [36].

With the advent of MDCT and in combination with the invaluable data provided by TEE, especially in intubated patients, we currently perform an accurate stratification of ATAIs according to the risk of aortic complications, and an early endovascular repair is performed whenever possible in all ATAIs except for aortic intramural haematomas with no identifiable intimal tears or small intimal tears <10 mm, which are the lowest risk subgroup in which indefinite delay in repair may be allowed [36].

In summary, the natural history of patients who are non-operatively managed has revealed a marked trend towards the development of late aortic-related complications, which may justify aortic repair, even in some low-risk patients. Moreover, the potential for the rapid progression of ATAIs in the same patients mandates serial radiological controls during the first three months after diagnosis and then annually thereafter.

2.7.7. Management of minimal aortic injuries

Minimal aortic injuries (MAI) include intimal tears <10 mm with minimal to no periaortic hematoma, whereas the remaining more severe aortic injuries or significant aortic injuries (SAI) consist of intramural hematoma without intimal tear, aortic transection / intimal tear > 10 mm, and aneurysm / pseudoaneurysm.

Nowadays MAI are being recognized more frequently due to the increasing use of high-resolution diagnostic techniques, especially with the increasingly widespread use of MDCT. In a recently published study [255], we found a 17.3% of MAI among the overall 52 ATAI in major trauma patients. This proportion was higher than the 10-13% of MAI among overall ATAI reported by other authors in other series of MAI [11, 116, 252]. In fact, 4 cases were diagnosed using dual slice helical CT during the period 2000-2006, whereas the MDCT diagnosed 5 patients in the period 2006-2011.

We have recently described [255] that the severity of major trauma is not usually lower in trauma patients sustaining a MAI than in trauma patients with SAI. On the contrary, in our series major trauma patients with MAI presented a worse prognosis and a higher expected mortality on admission than SAI patients as estimated by ISS, RTS and TRISS data [255]. Aortic injuries with other associated traumatic injuries must be evaluated altogether in the context of the multisystem impairment of major trauma patients given that these associated injuries can be just as lethal as the ATAI. This emphasizes the fact that treatment priorities should be modulated on an individual basis. In our aforementioned series [255], in-hospital mortality in major trauma patients with SAI (30.2%) was slightly higher than in major trauma with MAI (22.2%), although this difference did not reach statistical significance.

MAI may be the most amenable aortic injuries for non-operative management [36, 116, 255]. In contrast to SAI traumas, in-hospital mortality in MAI is not usually related to the aortic injury. Some authors have identified the potential adverse evolution of MAI as formation, enlargement, and rupture of pseudoaneurysm; embolism of loose intima, or thrombus; and progressive dissection of the aortic wall [116, 252]. In our series, the 85.7% of surviving MAI have spontaneously healed and only one patient has developed a small pseudoaneurysm without reaching indication for surgical repair [211]. Therefore, management of MAI must be conservative, but performing a close imaging surveillance to early detect a potential adverse evolution of the MAI, highlighting the risk of development of an aortic pseudoaneurysm.

2.7.8. ATAIs in crush trauma

Traumatic aortic injury is not a common injury, but aortic injury as the result of crush trauma is extremely rare [256]. Most of the published traumatic aortic injury series [15, 22, 32, 78] do not report ATAIs in crush trauma patients but mainly refer to deceleration trauma patients in either vehicle collisions or falls. Even in large series of crush trauma patients, the incidence of ATAI is remarkably low. Out of 215 acute thoracic crush trauma victims of the Sichuan (China) earthquake in 2008 evaluated by MDCT, only 1 patient (0.5%) presented with a traumatic aortic injury [257, 258].

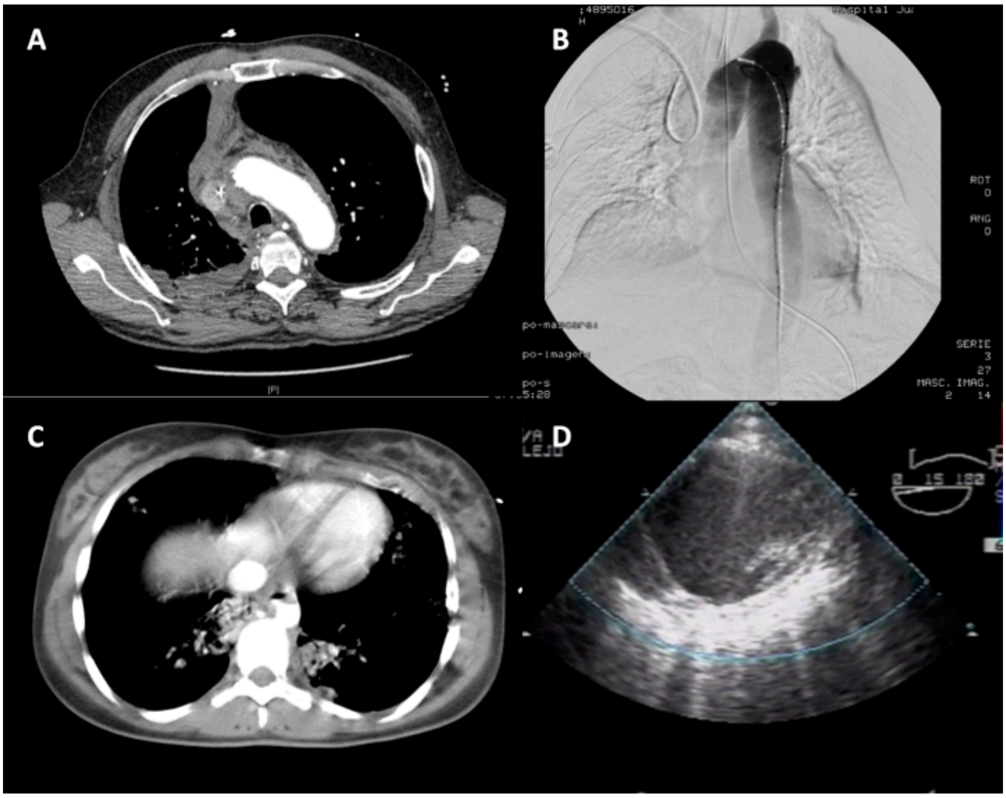


Figure 21. Test images of ATAIs caused by crush traumas. A. CT scan axial slide showing an aortic arch type II injury in a 66-year-old male crushed under a tractor. **B.** Aortography showing a small type I injury in a 34-year-old male crushed under a caterpillar tractor. **C.** CT scan axial slide showing a mid-descending aorta type I injury in a 40-year-old male crushed under a concrete block. The transesophageal echocardiogram (**D**) confirmed a small type I injury.

We published one of the largest series of ATAIs in crush traumas in the literature [256]. In our series, 6.8% of all ATAIs occurred as a result of being crushed under weight. Moreover, we found out that aortic injuries in crush trauma patients most frequently present as low-risk injuries and differ from ATAIs of non-crush trauma (deceleration or high-speed trauma) patients not only in radiological severity (Table 9; 100% vs. 43.5% of low-risk injuries, $P<0.05$) but also in aortic location, where the mid- and distal aorta and the aortic arch are more frequently affected [256].

Type of aortic injury	All patients (n=74)	Crush trauma group (n=5)	No-crush trauma group (n=69)	*p value*
Type I (Intimal tear)	17 (23%)	4 (80%)	13 (18.8%)	0.015
Type II (Intramural hematoma)	18 (24.3%)	1 (20%)	17 (24.6%)	
Type III (Aneurysm/ pseudoaneurysm)	3 (4%)	0	3 (4.3%)	
Type IV (rupture)	36 (48.7%)	0	36 (52.3%)	

Table 9. Types of aortic injury in crush trauma and non-crush trauma patients [256].

A tendency towards a higher rate of rhabdomiolysis, as determined by a higher peak in plasma CPK, and an increased risk of developing ARI in crush trauma patients have also been found [256]. Given that renal function can also be jeopardized by either open surgery or aortic endografting and considering the aforementioned higher incidence of low-risk aortic injuries among crush trauma patients, this subset of trauma patients would be better managed by a conservative approach to ATAIs whenever a low-risk aortic injury is diagnosed.

In summary, aortic injuries in crush thoracic trauma patients seem to present in different clinical scenarios to aortic injuries from high-speed thoracic trauma and may potentially require their own distinct considerations. The increased risk of rhabdomiolysis, subsequent acute renal injury and possible acute renal failure, as well as a tendency towards developing lower-risk aortic wall injuries, must be considered when planning the initial management of aortic injuries in crush trauma victims.

2.7.9. Ascending aorta and aortic arch traumatic injuries: a different challenge

The aortic isthmus is by far the most common site of ATAI, but up to 10% of cases of ATAI occur in atypical locations, including the aortic arch, the ascending aorta and the peridiaphragmatic aorta [10, 32, 78]. Among these atypical sites of ATAI, ascending aorta and aortic arch injuries stand out because of their ominous prognosis. Blunt traumatic injuries of the ascending aorta and the aortic arch present a different epidemiological profile than traumatic injuries at other aortic levels regarding prognosis, management and the number and distribution of associated injuries.

Traumatic injuries of the ascending part of the aorta and aortic arch branches are more common in penetrating trauma, whereas injuries of the isthmus and mid-descending or abdominal aorta are much more frequent in blunt trauma [21]. In unpublished series (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*) traumatic injuries of the ascending aorta and the aortic arch represented 20% of the 85 major trauma patients with ATAI included in that series (4 ascending aorta (4.7%) and 13 aortic arch (15.3%) injuries) (Figure 22). This represents a slightly higher proportion of injuries of the ascending aorta/arch than reported in other clinical studies.

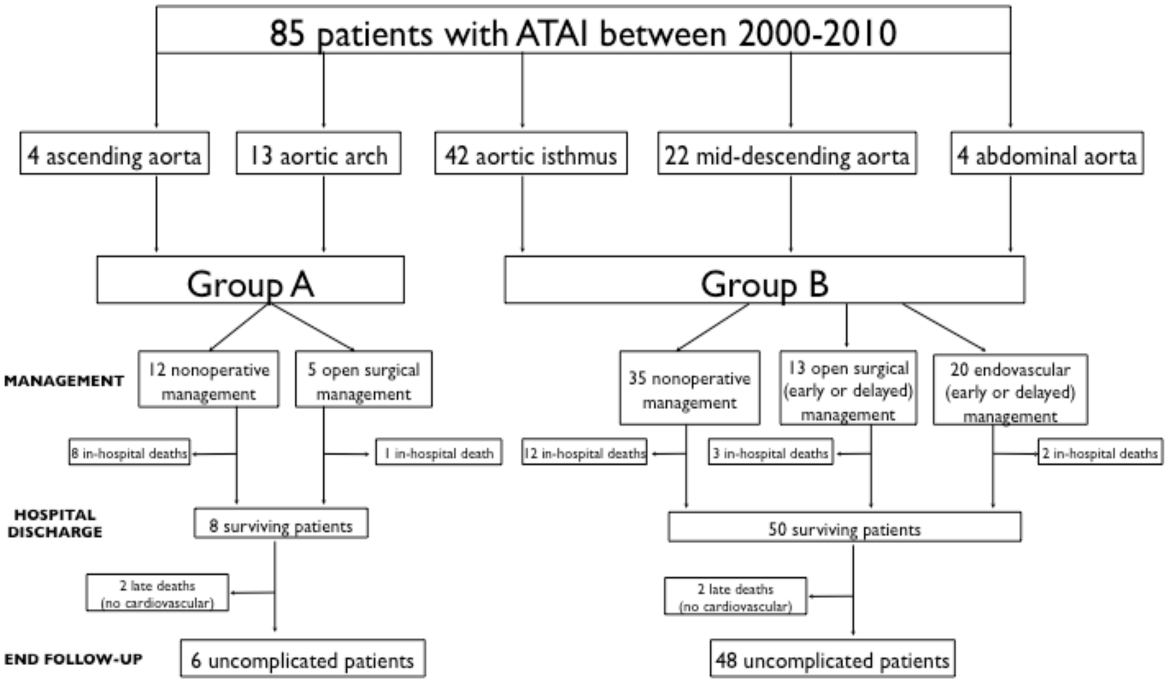


Figure 22. Flow chart showing the distribution of the 85 patients enrolled in a multicentre study of ascending aorta and arch injuries by Mosquera et al. (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*)

The site of ATAI was similar in the two multicentre studies sponsored by the *American Association for the Surgery of Trauma* and involved the ascending thoracic aorta/aortic arch in 7% in the $AAST_1$ study [25] and 5.4% in the $AAST_2$ study [15, 16]. Likewise, Cardarelli et al. published their experience managing ATAIs and reported only 2 ascending aorta and no arch injuries among 219 patients with blunt traumatic aortic injury [259].

In 1990, Eddy et al. [76] reviewed a series of 104 patients admitted to Harborview Medical Center with ATAIs over a 15-year period (1975-1990) and reported no ascending aorta traumatic injuries and 7 patients (7%) with arch injuries. In 2006, Cook et al. published a series from the same institution from 2000 to 2005, and only reported 1 ascending aorta and 3 patients (5.7%) with arch injuries among 54 patients with ATAIs [32]. The authors suggested that advances made in restraints might be responsible for the reduction in the incidence of ascending aorta and arch traumatic injuries when the two time periods were compared [32].

Aortic arch injuries are remarkably more frequent in autopsy studies than in clinical practice. In a large autopsy series published by Dosios et al., the analysis of time of death with regard to the anatomical location of ATAIs revealed that a greater percentage of victims with injuries of the isthmus or distal descending thoracic aorta reached the hospital alive compared to those injured at the ascending part of the aorta or aortic arch [21]. This series reported 57 ascending aorta (21.6%) and 18 aortic arch (8.3%) traumatic injuries out of 217 blunt trauma autopsies [21]. More recently, Teixeira et al. reported a series of 104 fatal blunt trauma victims with associated ATAIs, of which 3% were located at the ascending aorta and 11% at the aortic arch [22].

After demonstrating that the incidence of injury at the aortic isthmus in autopsy studies was lower than that demonstrated in clinical studies, several authors suggested that non-isthmus injuries of the aorta are more lethal [21-24]. Both relevant clinical and autopsy series seem to concur with the very poor prognosis of traumatic ascending aorta and aortic arch injuries. Eddy et al. reported an in-hospital mortality rate of traumatic injuries of the ascending aorta/aortic arch as high as 81% between 1975 and 1990 [76], whereas it decreased to a 33% in the series published by Cook et al. between 2000 and 2005 [32]. In our unpublished series (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*), the in-hospital mortality rate for ascending aorta or aortic arch injuries was significantly higher than the in-hospital mortality rate for injuries of the isthmus, descending thoracic or abdominal aorta (52.9% vs. 26.5%; *P*=0.036). Indeed, patients with ascending aorta or arch injuries presented a higher mortality rate than expected on admission, as reflected by both significantly higher TRISS (59.7±38.6 vs. 36.6±35.3; *P*=0.20) and ISS (48.2±21.6 vs. 39.4±14.6; *P*=0.048).

In our unpublished series, the survival rate was 46.3% at 1 year, 38.6% at 5 years and 19.3% at 10 years in major trauma patients with ATAIs at the ascending aorta or the aortic arch, whereas the survival rate was 75% at 1 year, 73.2% at 5 years, and 69.1% at 10 years in major trauma patients with an aortic injury at a more distal location (isthmus and descending or abdominal aorta) (Figure 23). A significantly shorter long-term survival was found in patients with traumatic injury of the ascending aorta or aortic arch (Log-rank test *P*=0.003).

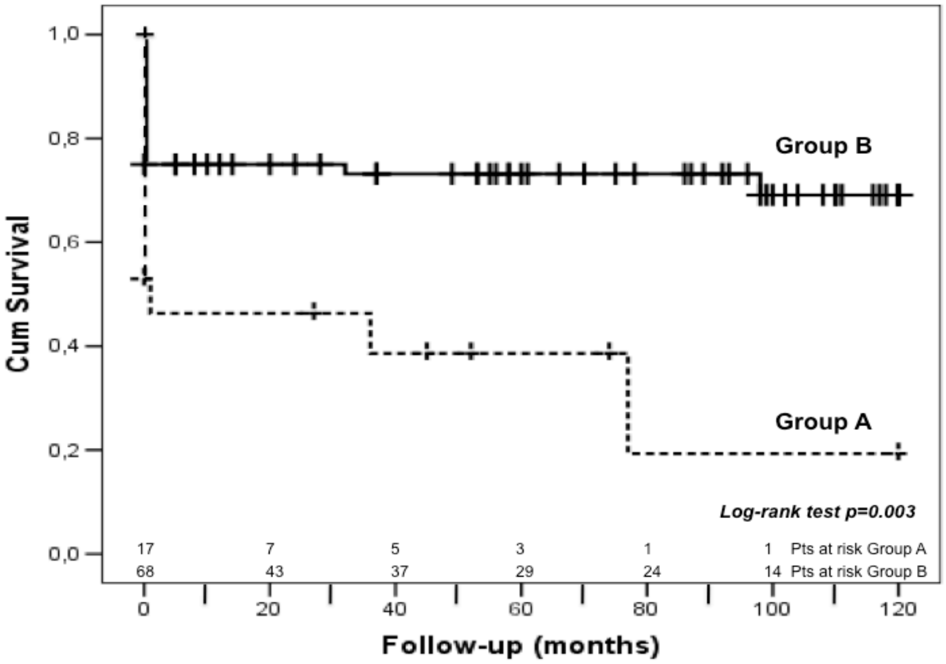


Figure 23. Kaplan-Meier survival curves of traumatic aortic injuries of the ascending aorta or the aortic arch (group A) vs. traumatic aortic injuries of the aortic isthmus, mid-descending aorta or abdominal aorta (group B) (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*).

The grave immediate prognosis of injuries located at the ascending aorta and aortic arch is probably the result of frequent lethal concomitant intrathoracic injuries. In our series (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*), associated thoracic traumatic injuries included myocardial contusion and haemopericardium in 41.2% and 35.3% of ascending aorta and arch cases, respectively, but in patients with traumatic aortic injuries at other locations there were only 11.8% and 8.8%, respectively. We also found that the distribution of coexisting extrathoracic injuries was dissimilar between ascending aorta/arch injuries and aortic injuries at other locations, where the former included a significant number of extrathoracic injuries. Severe head and neck injuries (AIS>3) and spinal cord injuries were more frequent in patients with traumatic ascending aorta/arch injuries. In the group of patients with ascending aorta/arch injuries, the cause of death was directly related to the traumatic aortic injury in only five cases (55%), and head and abdominal injuries were the cause of death in the remaining four cases (45%). This emphasizes the fact that associated injuries can be just as lethal as the aortic injury, and that treatment priorities should be modulated on an individual basis.

During the last decade there have been several substantial diagnostic and therapeutic advances which have changed the management of thoracic aortic injuries. The advent of thoracic aorta endografting and the delay in surgical treatment after the stabilization of associated critical injuries have enabled a revolution in the management of ATAIs in major trauma patients, leading to a reduction in the in-hospital mortality rate in most recent series. However, in no series published in the literature has endovascular treatment been found to improve the prognosis of traumatic injuries of the ascending aorta or the aortic arch [36]. Nevertheless, the spread of hybrid surgery, which is gaining use by surgeons treating complex non-traumatic aortic arch pathologies [260, 261], may allow surgeons to treat traumatic arch injuries that would otherwise be inoperable and to reduce the operative mortality of such complex traumatic injuries. Although the contribution of aortic endografting to the treatment of traumatic ascending aorta and aortic arch injuries was minor, improved trauma care, pre-hospital resuscitation, the widespread use of computed tomography as a screening tool [60] and clinical management with aggressive blood pressure control [36] have reduced the mortality rate of these injuries over the last few years, as reported by several authors [16, 32, 78].

The definitive management of traumatic injuries of the ascending aorta or the aortic arch usually involves an open surgical repair (five cases in our series, 29.4%), which is associated with a significant rate of surgical mortality (one case in our series, 20%) [32, 76, 191, 262]. In our series (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*), 12 patients (70.6%) received non-operative management. In general, indications for a conservative approach are low-risk aortic injuries (intimal tear or intramural haematoma without a tear) [33, 81] or high-risk patients with severe associated non-aortic traumatic injuries, comorbidities or advanced age. In our unpublished series (*Unpublished data, Mosquera, V.X. Under review. See Appendix II*), among the 12 patients with ascending aorta/arch injuries and conservative management, 3 patients with high-risk ATAI (transection/rupture or pseudoaneurysm) died because of aorta-related complications and 5 patients died because of extrathoracic injuries. Despite significantly shorter long-term survival in patients with ascending aorta/arch injuries, none of the 4 surviving patients in this group with low-risk injuries experienced any aortic-related complications thanks to a strict control of blood pressure and cardiac contractility and a close imaging surveillance.

In summary, traumatic aortic injuries of the ascending aorta and aortic arch seem to present a different clinical profile than “typical” isthmus injuries with a higher incidence of both intrathoracic and neurological injuries. Beyond the high aortic-related in-hospital mortality of the ascending aorta and arch injuries, these patients’ associated injuries can be just as lethal as the aortic injury, and treatment priorities should be modulated on an individual basis. The advances in trauma care and pre-hospital resuscitation, as well as in diagnostic tests, have improved the poor prognosis of these patients. Although the advent of TEVAR has had a negligible impact in the treatment of ascending aorta and arch traumatic injuries compared to the revolution experienced in the treatment of isthmus and descending aorta, the spread of aortic hybrid surgery may pose an attractive alternative treatment for complex arch injuries.

2.7.10. Management of ATAIs associated with major aortic abdominal visceral branch injuries

Acute traumatic aortic injuries associated with injuries to major aortic abdominal visceral branches (MAAVBs) are an uncommon but highly lethal situation among major blunt trauma patients. The in-hospital mortality rate in this critical subset of major trauma patients can vary between 50% to 100% [263, 264], where exsanguinating haemorrhage is the most important cause of early death [265, 266]. The vast majority of this subset of major trauma patients present in shock, with severe physiological compromise and multiple injuries, subsequently developing acute renal failure, abdominal malperfusion syndrome and/or coagulopathy [266-268]. Intra-abdominal vascular injuries are associated with extremely rapid rates of blood loss and pose a surgical challenge for exposure during celiotomy [267, 269, 270], given the posterior position of the MAAVBs.

The management of injuries to MAAVBs can vary from a conservative to an endovascular or an open surgical treatment. Conservative treatment includes blood pressure control and close clinical (urine output, CPK levels, creatinine serum levels, metabolic acidosis) and imaging (focused assessment with sonography for trauma (FAST) and CT scanning) surveillance.

The advent of different endovascular therapies for the treatment of both ATAIs [15, 238-241] and injuries to visceral arteries [271-276] has enabled a revolution in the management of these catastrophic injuries among major trauma patients, leading to a decrease in the in-hospital mortality rate in most recent series. Early angiography and embolization or stenting for treating an injury to an MAAVB should be initiated at the discretion of the attending surgeon, especially as first staged therapy of life-threatening bleeding, when the uncontrolled bleeding persisted immediately postoperatively after open repair or as an adjunct to damage control.

In the open repair of MAAVB injuries, once exposure and proximal and distal control have been achieved, the routine principles of vascular surgery should be applied, including debridement of the vessel wall, the prevention of embolization caused by a clot or plaques, irrigation with heparinized saline, embolectomy with a Fogarty catheter, arteriorraphy with a monofilament vascular suture or the interposition of autologous or prosthetic grafts, and the initiation of early damage control [267, 277].

An association between aortic wall and visceral artery injuries typically appears in penetrating abdominal trauma and the segment of the aorta affected is usually the abdominal aorta [277]. However, this combination of vascular injuries is seldom reported in blunt thoracoabdominal trauma. Asensio et al. [277] presented the largest series published in the literature of abdominal vascular injuries, including both penetrating and blunt trauma, with a total of 302 patients. In this series, only 17 cases of abdominal aortic injury were associated with another abdominal vascular injury, most of which occurred in penetrating traumas. The in-hospital mortality rate in these 17 patients reached 82.4% [277]. More recently, Teixeira et al. reported an autopsy series of 102 major trauma victims with ATAIs, among which only four patients (3.9%) had associated visceral vessel injuries [22]. In a recently published study from our institution [278], we found that 19.2% of the 52 major blunt trauma patients with ATAIs admitted to our institution during the last decade sustained an associated injury to the MAAVBs. Moreover, it must be noted that in half of these patients [278] with associated MAAVB injuries the ATAI was located in the thoracic aorta, being either in the isthmus or mid-descending thoracic aorta, which differs remarkably from other series.

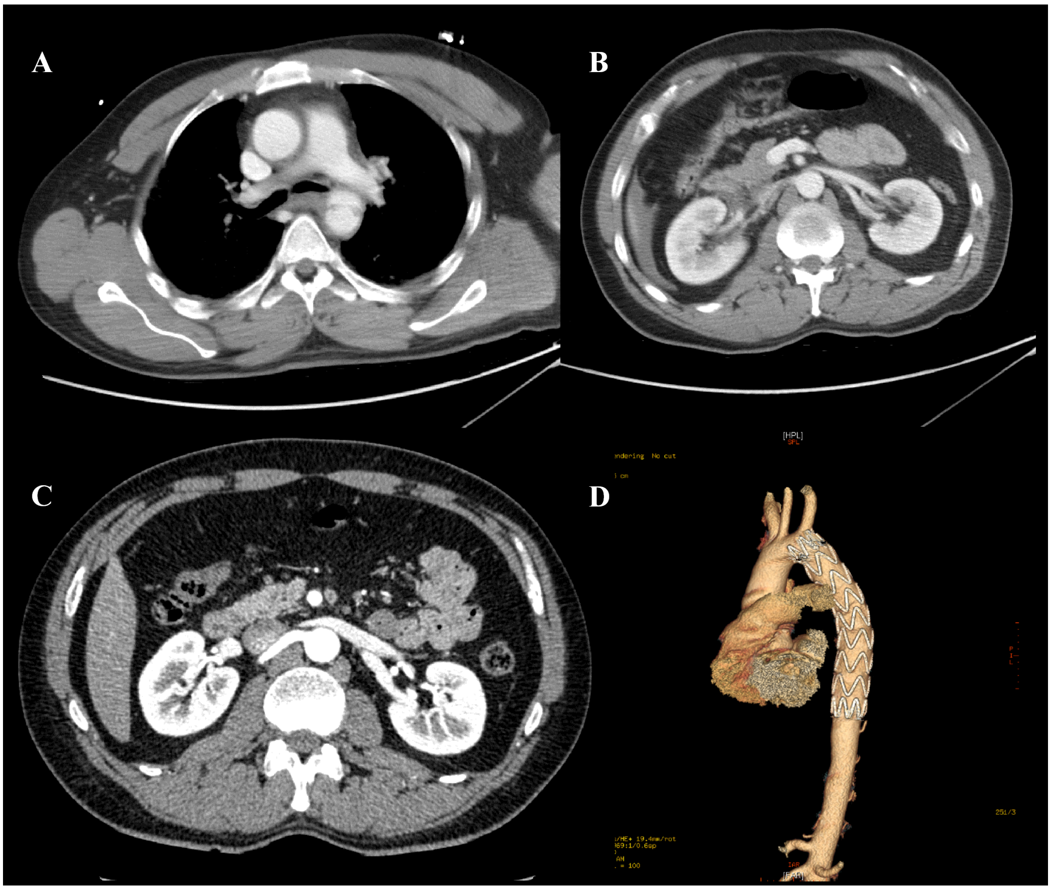


Figure 24. MDCT on admission and after 1 week in a major trauma patient with associated ATAI and MAAVB. ***A.*** Thoracic MDCT axial slide showing the aortic transection at the isthmus level. ***B.*** Abdominal MDCT axial slide demonstrating a right renal artery dissection that was conservatively managed because its blood flow improved after TEVAR. ***C.*** Abdominal MDCT axial slide after 1 week, confirming the improvement in right renal artery blood flow. ***D.*** Three-dimensional thoracic MDCT reconstruction after 1 week, showing complete exclusion of the aortic injury after TEVAR [278].

Major blunt trauma patients with associated ATAI and MAAVB injuries pose a great surgical challenge. The majority of these patients present in shock, are physiologically compromised, sustain multiple associated non-vascular injuries and significant blood losses, and their mortality rate remains extremely high. Few series have specifically focused on the management of both concomitant types of injuries. In our series [278], all patients with ATAI and MAAVB injuries presented with a severe non-vascular associated injury (AIS>3), at least. In addition, major trauma patients with associated ATAI and MAAVB injuries presented with haemodynamic instability more frequently than patients without combined vascular injuries. In fact, we found that hypotension was significantly more frequent in patients with aortic and MAAVB injuries (100% vs. 66.6%, P=0.04) [278].

Major blunt trauma patients with concomitant aortic and MAAVBs injuries are also associated with high rates of morbidity and require a more hazardous management at the ICU. We found a significantly higher mean peak CPK in the group with combined ATAI and MAAVB injuries than in the group without an associated MAAVB injury (23008±33400 IU/l vs. 3970±3495 IU/l; P<0.001) [278]. This finding may be explained by an increased tissue necrosis secondary to malperfusion syndrome and rhabdomiolysis in this critical subset of trauma patients. Furthermore, ATAI patients with associated MAAVB injuries presented with a higher rate of ARIs (50% vs. 26.2%, P=0.27), requiring more frequent haemodiafiltration [278].

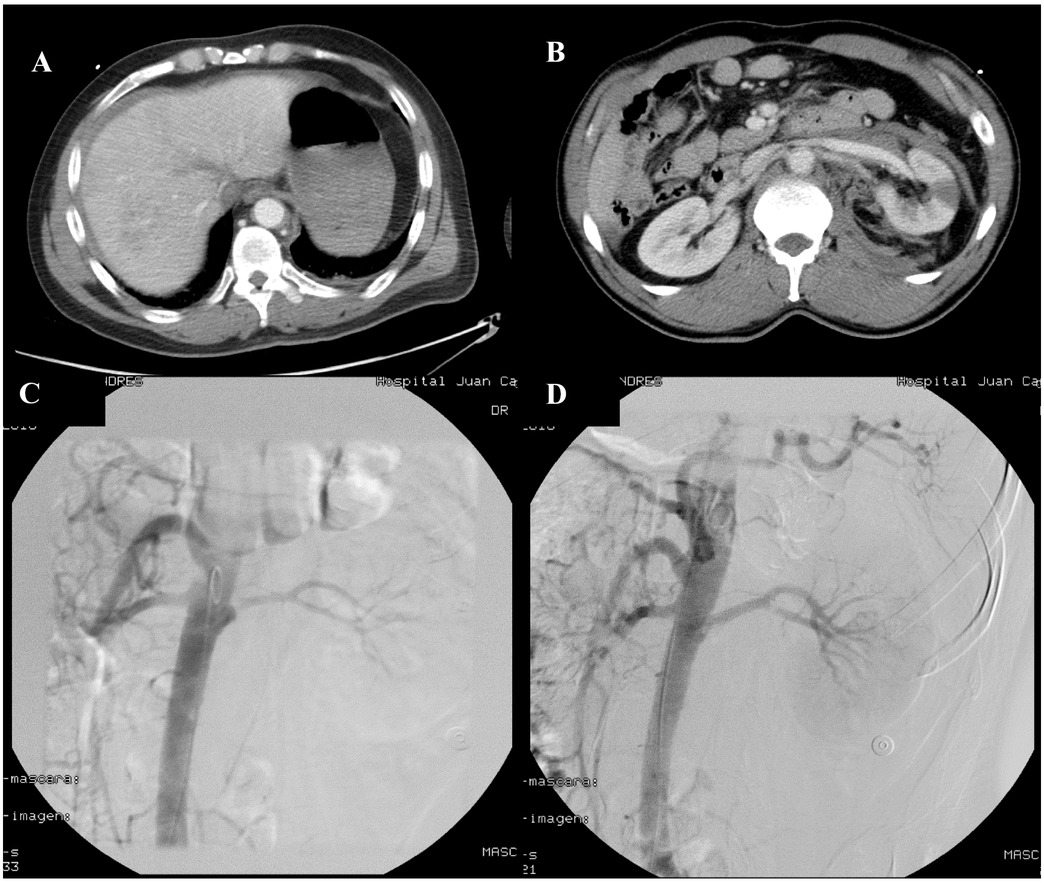


Figure 25. On admission MDCT and aortography images from a major trauma patient with associated ATAI and MAAVB. A. An intimal tear can be observed in the abdominal MDCT axial slide from the time of admission. **B.** The abdominal MDCT axial slide also shows an left renal artery perfusion defect due to an intimal flap. **C.** Emergent abdominal aortography confirms the lack of perfusion in the left kidney. **D.** Control abdominal aortography after the deployment of a 7 mm stent in the left renal artery. Notice the complete restoration of blood flow in the left renal artery [278].

In-hospital and long-term mortality rates in major trauma patients with associated ATAI and MAAVB injuries are higher than in major trauma patients with ATAIs who did not suffer concomitant injuries to the MAAVBs [278]. Nevertheless, in our aforementioned study [278], we observed that the in-hospital mortality rate tended to be lower than the expected mortality by TRISS in both groups of major trauma patients.

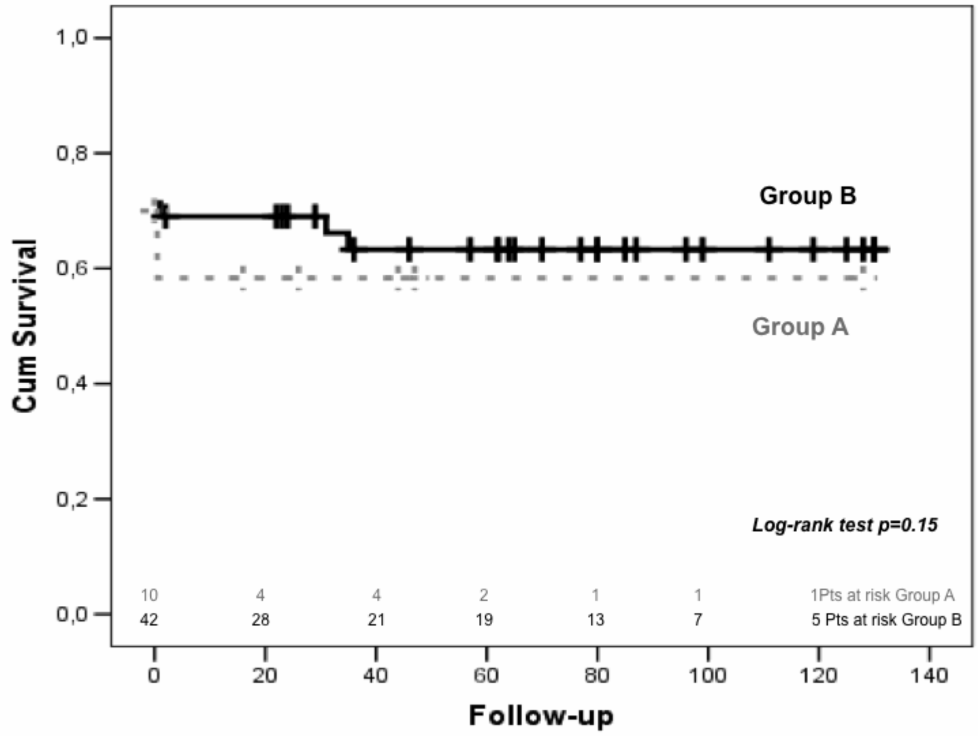


Figure 26. Kaplan-Meier survival curves of ATAI patients with associated MAAVB injuries (group A) and ATAI patients without associated MAAVB injuries (group B), including in-hospital mortality [278].

These satisfactory outcomes in patients with ATAIs, especially in the most critical subset of major trauma patients, are due to a multidisciplinary approach combining endovascular and open surgical techniques for the staged treatment of life-threatening aortic and visceral vascular injuries. The multidisciplinary approach for the management of the latter includes early embolization or stenting, early surgical intervention to control haemorrhaging, damage control, the use of early packing and staged surgical procedures. Several series have reported the use of stenting and angioembolization as adjuncts to the non-operative management of blunt vascular visceral injuries, and/or as means of avoiding surgical intervention [271-276]. In some cases, we advocate for an early endovascular management, with either stenting or angioembolization of the visceral vascular injury, followed by an open surgical approach [278]. According to our experience, nephrectomy may be required after renal angioembolization for grade IV-V of the renal Organ Injury Scale (OIS), as previously reported by other authors [279].

In summary, associated aortic and MAAVB injuries in major trauma patients seem to present in different clinical scenarios. These patients present with an increased risk of rhabdomiolysis, visceral ischaemia and acute renal failure, as well as a higher in-hospital mortality rate. A multidisciplinary approach combining endovascular and open surgical techniques for the staged treatment of these life-threatening aortic and visceral vascular injuries is mandatory in this critical subset of trauma patients.

BRIEF SUMMARY

In major trauma patients with associated ATAIs, the initial assessment follows the principles of the Advanced Trauma Life Support protocol. In unstable patients, the repair of a contained aortic rupture is third in the hierarchy when addressing life-threatening injuries, where addressing an ongoing haemorrage comes first regardless of the source and the treatment of any intracranial haemorrhage causing a mass effect comes second.

Haemodynamic monitoring and medical therapy should be initiated whenever there is a suspicion of ATAI in a major trauma patient. Medical therapy should include intravenous infusion of a vasodilator to avoid hypertension and the limitation of intravenous fluid infusion. Systolic blood pressure should be titrated to approximately 100 mmHg, and the heart rate to <60 bpm. The first-line medical treatment for ATAIs is intravenous beta-blockers.

Conventional open repair of ATAIs with the interposition of a graft has been the standard with which all other management strategies should be compared; it has been proven to be safe and durable. Risk factors for postoperative paraplegia include increased cross-clamping time, the length of the aorta that is excluded, a low distal perfusion pressure, systemic hypotension, the number of intercostal arteries ligated, increased body temperature and increased cerebrospinal fluid pressure. The simple aortic cross-clamping (clamp-and-sew) technique has been used in the past, but it yielded higher rates of paraplegia than the techniques that use extracorporeal lower body perfusion.

Various perfusion techniques have been developed to reduce the incidence of paraplegia resulting from spinal cord ischaemia. Distal perfusion with the use of a passive shunt (Gott shunt) was found to shunt blood from the proximal aorta to the distal aorta depending on the pressure gradient.

The use of a centrifugal pump with heparin-bonded tubing and active partial left-heart bypass does not require systemic heparinization, maintains lower body perfusion, unloads the left heart and controls proximal hypertension, controls intravascular volume and enables active warming in cases of associated hypothermia. A full cardiopulmonary bypass enables active cooling and facilitates a period of hypothermic circulatory arrest, but it requires full systemic heparinization.

Several adjunctive measures can be used to reduce the risk of spinal cord ischaemia, namely, monitoring motor or somatosensory evoked potentials, lumbar cerebrospinal fluid drainage, hypothermia and neuroprotective pharmaceuticals.

Thoracic endovascular aortic repair (TEVAR) for ATAIs is a less-invasive and less time-consuming technique that avoids the potential morbidity of open repair. Paraplegia occurs in approximately 5.6% to 7% of patients after open surgery compared to less than 1% after TEVAR. However, TEVAR has not been prospectively studied for ATAI treatment, and US Food and Drug Administration-approved devices are being used “off label”. The follow-up requires CT angiography to be performed during the first postoperative week, at the time of discharge and at 1, 6 and 12 months. Potential complications that can occur after TEVAR include endoleak, stent-graft collapse, stroke, embolization, bronchial obstruction, migration, paralysis, dissection and rupture. Left subclavian artery revascularization must be individualized depending on the status of the vertebral anatomy in patients with ATAI who are undergoing TEVAR. The routine use of spinal drainage is not recommended by current clinical practice guidelines for TEVAR in ATAI, and it should only be used for symptoms of spinal cord ischaemia.

The delayed repair of stable ATAIs, irrespective of the presence or absence of major associated injuries, is associated with improved survival, but also with a longer length of ICU stay.

2.8. The rationale behind predictive scoring in ATAIs

The emphasis on improvements in prediction has become a hallmark of the quest of medical studies, and predictive literature is attracting increasing attention in medicine [280]. Nevertheless, the utility of this literature can be hampered by methodological limitations affecting design, analysis and reporting [281, 282].

Multivariate risk models are commonly used to assess the risk of specific cardiovascular diseases. Predictive risk modelling is essential for quality improvement activities in managed care systems, especially in cardiovascular medicine. It serves multiple purposes, such as provider profiling, cost containment, planning of resource allocation, patient counselling, planning of patient management and the construction of efficacy studies. The importance of risk models is such that their reliability and reproducibility in populations other than the one from which they were derived must be absolutely proven. Otherwise, any clinical and administrative decisions based on these models can be critically flawed by their instability in external populations.

Predictive scores are of a paramount importance as screening tools for rare but potentially lethal conditions such as ATAIs in major trauma patients. There are two remarkable facts that must be remembered about ATAIs. First, the vast majority of major trauma patients who suffer a high-degree ATAI (i.e. frank rupture) die at the site of the accident. Hence, the proportion of this pathology among surviving major trauma patients who arrive at hospital alive is relatively low. Second, ATAIs are overlooked at the initial screening in a significant percentage of patients due to the presence of more urgent life-threatening associated injuries such as intra-abdominal haemorrhaging or bleeding pelvic fractures.

The diagnostic performance of a test or the accuracy of a test for discriminating diseased cases from normal cases is evaluated using receiver operating characteristic (ROC) curve analysis [283, 284]. When we consider the results of a particular test in two populations, one population with a disease and the other population without the disease, we rarely observe a perfect separation between the two groups. Indeed, the distribution of the test results will most likely overlap, as shown in Figure 27.

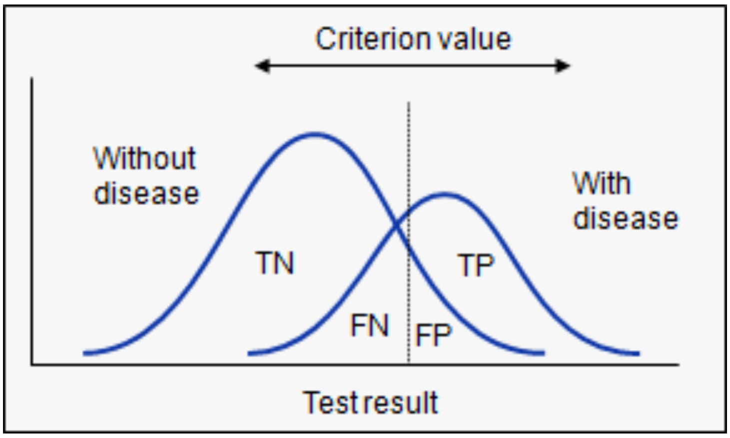


Figure 27. Selection of a criterion value. The overlap between both populations (with and without the disease) depending on the value of the selected criterion.

For each possible cut-off point or criterion value we select to discriminate between the two populations, there will be some cases where the disease is correctly classified as positive (TP = true positive fraction) and some cases where the disease will be classified as negative (FN = false negative fraction). On the other hand, some cases without the disease will be correctly classified as negative (TN = true negative fraction), but some cases without the disease will be classified as positive (FP = false positive fraction).

One challenge is to demonstrate that new candidate predictors can offer independent, incremental information beyond what is already known based on traditional risk factors [280, 285]. A sophisticated new predictor may have good predictive ability on its own, but it might not improve the predictive ability further when simple, easy-to-measure traditional factors are already taken into account [280].

When developing a predictive score for an uncommon but potentially lethal condition such as traumatic aortic injury, it is vital to strike a balance between a high sensitivity and an acceptable level of specificity.

If a high criterion value is selected, the false positive fraction will decrease with increased specificity but, on the other hand, the true positive fraction and sensitivity will decrease (Figure 28).

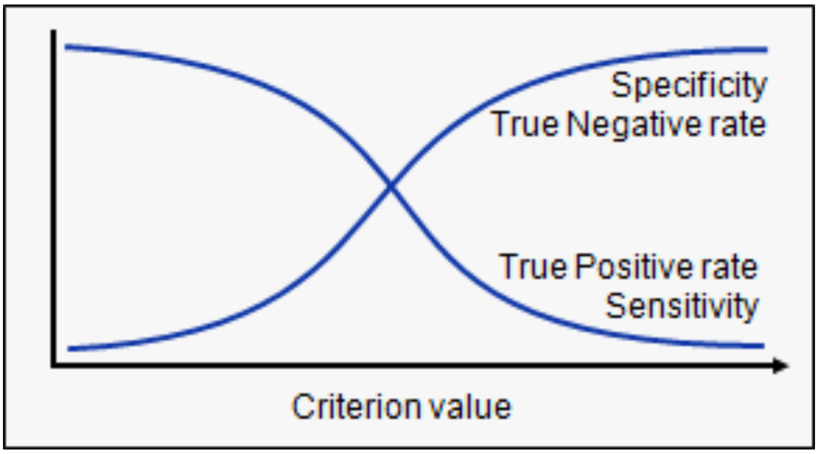


Figure 28. Sensitivity and specificity depending on the selected criterion value. The diagram shows that the higher the criterion value chosen, the greater the specificity will be. In contrast, the higher criterion value we use, the lower the sensitivity we obtain.

A low criterion or cut-off value will guarantee a higher rate of true positives (sensitivity) but with a detrimental effect on specificity. Although it may be sensible from a purely clinical point of view, this has led to growing concern about the potentially detrimental effects of obtaining additional images. Patients who are exposed to radiation incur a small associated risk of cancer [286]. Patients, institutions and society as a whole assume the added economic burden of obtaining and interpreting these studies [127, 287].

On the other hand, a high cut-off value will miss an important number of positive cases (false negatives) with the inherent risk of misdiagnosing a highly lethal condition, which is not affordable from a clinical point of view.

Regression analysis are the analytic techniques most commonly used for predictive risk modelling. However, the resulting models are only useful if they reliably predict outcomes for patients by determining significant risk factors associated with the outcome of interest. Problems can arise from this dependence on risk factor analysis. Different investigators evaluating the same predictors through regression analysis might obtain different results because of methodological discrepancies and inadvertent biases introduced in the statistical analysis [288]. Hence, it is of the utmost importance that all predictive score models are validated before general use.

Like any scientific hypothesis, the generalizability of a prognostic system is tested for accuracy across increasingly diverse settings. The more numerous and diverse settings in which a system is tested and found to be accurate, the more likely it will be able to generalize in an untested setting. Before adopting a new prediction model it is important to evaluate its “generalizability” in two ways [289]. First, one should evaluate the “reproducibility” of the predictive model among the patients included in the development model (internal validation). Second, in order to evaluate “transportability,” the accuracy of the model’s predictions should be examined in a new patient population with the same disease but with different enrolment methods and patient characteristics.

Internal validation can be accomplished by either the traditional training-and-test method or by the more recent bootstrap method. The traditional training-and-test method for model building, consisting of a random splitting of the database into a derivation set from which the model is constructed and a test set for assessing its calibration and discrimination, might be subject to sampling noise. Bootstrap analysis was recently proposed as a breakthrough method for the internal validation of surgical regression models [290, 291]. The main advantage of this technique is that the entire dataset can be used to build the model, enabling the construction of more robust models, especially in moderately sized databases and for rare outcomes (i.e. ATAIs in major trauma patients). Furthermore, the predictive validity of the model can be assessed not only in one randomly split set of patients but also typically in 1,000 new, different samples of the same number of patients as the original database obtained by resampling with replacements. Furthermore, a more accurate confirmation of the applicability of a predictive model in different geographic areas requires an external validation process [289]. External validity is assessed applying the predictive model to an independent population, which should be different from the target study population used to build the prediction model.

In our current study the predictive score was designed to rapidly identify major trauma patients at high risk of suffering an ATAI and to provide a framework to optimize resource use and to initiate prompt medical management in order to prevent potentially lethal aortic-related complications. According to the validation requirements of the aforementioned model, we performed an internal validation using the bootstrap method and an external validation applying the model to an independent multicentre database.

BRIEF SUMMARY

Predictive risk modelling is essential for quality improvement activities in managed care systems, especially in cardiovascular medicine. New candidate predictors should be able to offer independent, incremental information beyond what is already known based on traditional risk factors

Regression analyses are the analytic techniques most commonly used for predictive risk modelling. Before adopting a new prediction model, it is important to evaluate its “reproducibility” among the patients included in the development model (internal validation) and its “transportability”, where the accuracy of the model’s predictions should be examined in a new patient population with the same disease but with different enrolment methods and patient characteristics. Internal validation can be accomplished by either the traditional training-and-test method or by the more recent bootstrap method. External validity is assessed applying the predictive model to an independent population.

3. SCOPE, OBJECTIVES AND MOTIVATION OF THE RESEARCH

The first review of both our institutional results and the literature published to date about ATAI management revealed that long–term outcomes of certain uncommon types of ATAI (crush trauma aortic injuries, minimal aortic injuries, ascending aorta and aortic arch injuries or ATAI associated with other aortic branch injuries), as well as the safety and outcomes of conservative management, were poorly documented. Most studies only focused on isthmic injuries and on operative management, either endovascular or open repair, there being a lack of information about the outcomes of patients with “atypical or non-isthmal” injuries, non-decelerating mechanisms of injury and patients managed non-operatively.

As we have mentioned in *sections 2.7.7, 2.7.8* and *2.7.9* of *chapter State of the art in ATAI*, our previous studies provided a new insight to outcomes of uncommon types of ATAIs, as well as to the results of conservative management. These studies shed some light on important and poorly explored topics about ATAIs in major trauma patients. Our previously published results also suggested that ATAIs are not diagnosed soon enough to start an effective management and to avoid potentially lethal aortic-related complications in a not negligible number of major trauma patients. Furthermore, the natural history of major trauma patients with ATAI presents a marked trend towards the development of late aortic-related complications, which may justify an early aggressive diagnostic management for risk stratification. This finding generated the main objective of this thesis: the development of an easy, fast and practical predictive scoring method for determining the risk of ATAIs in major trauma patients based on simple data provided by an initial clinical examination and CXR performed on trauma admission. Given that we were going to develop the scoring method using a population of major trauma patients from 1980 to 2010, it was extremely important to externally validate the model in a current population of major trauma patients from different geographical areas. In addition, it became obvious that we required an actualization of our strategies of management and treatment algorithms by combining our research findings with best international practice evidence.

Subsequently, the in-depth research of major traumas and ATAIs in our Spanish region, Galicia, demonstrated that there was little or no information about the epidemiology and differences in prognosis of ATAI among major trauma patients in our area, whose population was 2,797,653 inhabitants in 2010 (data provided by *Instituto Galego de Estadística*: http://www.ige.eu/web). Moreover, it had not been established whether the association of an aortic wall injury modified the prognosis of major trauma patients and to which degree. As a consequence of these unknown factors emerged the need to precisely define the epidemiology of ATAIs among major trauma patients in our region as an additional objective of this thesis research.

In conclusion, we may summarize the objectives of this thesis in as follows:

I. Objective I- Epidemiology of ATAI in Galicia

  - Estimating the global burden of ATAIs among major trauma patients in our institution and our region.
  - Defining the clinical profile of the major trauma patient sustaining an ATAI in Galicia.

- Assessing the influence of ATAIs on the early outcomes and prognosis of major trauma patients in terms of in-hospital mortality and length of hospital stay in Galicia.

II. Objective II- Predictive score of the risk of ATAI in major trauma patients

- Developing a predictive score of the probability of ATAIs among major trauma patients with associated blunt chest trauma.
- Performing an external validation of the predictive score in a current dataset of major trauma patients to test its applicability at the current time and in different geographical areas.
- Actualizing our current management protocols for major trauma patients according to the risk of presenting with an ATAI.

4. PATIENTS AND METHODS

4.1. Study designs and patient recruitment

For the purpose of the study, major trauma patients were defined as victims of trauma of sufficient energy to put them at risk of an important injury, associating blunt chest trauma or risk of chest injury, who were transported to a level 1 trauma centre and presented with an injury severity score (ISS) [292] greater than 15, as described in the published literature [292-294].

The major trauma patients who were enrolled in the study were classified into either the ATAI group (associated acute traumatic aortic injury) or the NATAI group (no associated acute traumatic aortic injury).

In order to achieve the objectives cited in the previous chapter, we developed 2 different study designs to accomplish the objectives of our thesis research:

4.1.1. Study design for Objective I (Epidemiology of ATAI in Galicia)

This first part of the research consisted in a retrospective descriptive study of all major trauma patients with blunt chest trauma admitted to a public hospital in Galicia from 2006 to 2010, followed by a comparison of the distinct clinical profile between trauma patients with and without an associated ATAI. We analysed data from all the public hospitals admitting trauma patients in Galicia, namely:

- *Complejo Hospitalario Universitario de A Coruña* (CHUAC).
- *Complejo Hospitalario Universitario de Vigo* (CHUVI).
- *Complejo Hospitalario Universitario de Santiago de Compostela* (CHUS).

- *Complejo Hospitalario Universitario de Ourense* (CHUO).
- *Complejo Hospitalario Universitario de Pontevedra* (CHUP).
- *Hospital Universitario Lucus Augusti* (HULA) (former *Complejo Hospitalario Xeral-Calde)*.
- *Hospital da Costa-Burela.*
- *Complejo Hospitalario Arquitecto Marcide-Ferrol.*

Only three of them (CHUAC, CHUVI and CHUS) are the level 1 trauma centres available in Galicia, Spain.

Major trauma with thoracic injury database from the whole Galician region in the period 2006-2010 was provided by the regional health system data department, *Unidade de Codificación Clínica, Servicio Galego de Saude* (SERGAS). This department supports an administrative database containing inpatient admissions gathered from all public hospitals in Galicia that comprises all admissions in Galicia since 2006. The diagnosis and relevant procedures from all discharges are coded by a team of specifically trained physicians. The database was queried for all adult patients (age >15 years old) with blunt thoracic major trauma utilizing the codes from the International Classification of Diseases, 9th revision (ICD-9) (Table 10). According to the internationally accepted definition of major trauma (ISS>15), 1,760 adult (>15 years old) blunt major trauma patients (involving the chest) were admitted to public hospitals in Galicia in the period 2006-2010, of whom 44 sustained an ATAI.

ICD-9 codes screened for identification of major blunt chest trauma patients

Traumatic hemothorax 860.2-860.5

Brain injury 850.3-850.5, 850.9, 851-854.x

Heart injury 861.0-861.1x

Lung injury 861.2-861.3x

Abdominal injury 863-869.x

Major orthopedic injury 805.x, 806.x, 808.x, 820.x, 821.x

Thoracic blood vessels injury 901.x

- ***901.0 Thoracic aorta***
- 901.1 Brachiocephalic and/ or subclavian arteries
- 901.2 Superior vena cava
- 901.3 Innominate and/or subclavian veins
- 901.4 Pulmonary vessels injury
  - 901.40 Not specified pulmonary vessel
  - 901.41 Pulmonary artery
- 901.42 Pulmonary vein
- 901.8 Other thoracic vessels
  - 901.81 Intercostal artery or vein
  - 901.82 Internal thoracic artery or vein
  - 901.83 Multiple thoracic vessels
  - 901.89 Azygos/ Hemiazygos vein
- 901.9 Not specified thoracic vessel injury

Table 10. ICD-9 codes screened for identification of major blunt chest trauma patients (ICD-9, International Classification of Diseases, 9th Revision).

In summary, for this first part of the research all the major trauma patients admitted to a public hospital in Galicia between years 2006 and 2010 were enrolled, accounting for a total of 1,760 major trauma patients, of whom 44 sustained an ATAI as shown in Figure 29.

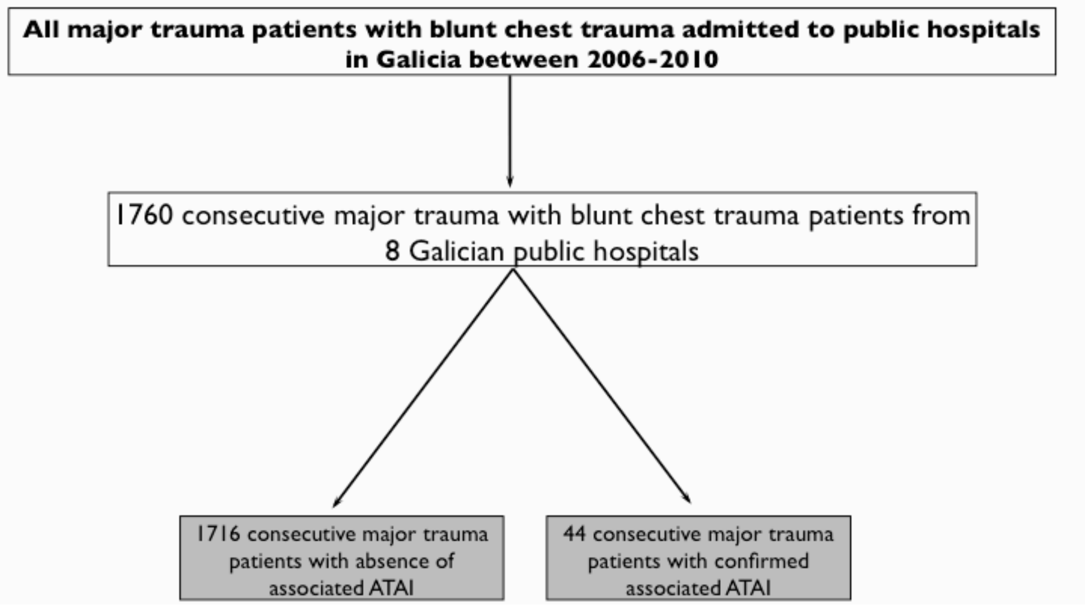


Figure 29. **Design of the descriptive retrospective study for recruitment of overall major trauma patients with associated blunt chest injury in Galicia between 2006 and 2010.**

4.1.2. Study design for Objective II (Predictive risk scoring method)

The second part of the research was a cross-sectional study of a diagnostic procedure. The development of a predictive score for the risk of ATAI in major trauma patients with blunt chest trauma was carried out in two stages. In the first stage, we analysed the clinical and radiological characteristics of major trauma patients in order to develop the screening tool for ATAIs among major trauma patients. In the second stage, we validated the predictive score in an independent external population of major trauma patients.

In the predictive score development, the overall study population consisted of 640 major trauma patients (all of them with blunt chest trauma) divided into two datasets: a score dataset provided only by the *Complejo Hospitalario Universitario de A Coruña* (CHUAC), and an independent validation dataset provided by other three different institutions: *Complejo Hospitalario Universitario de Vigo* (CHUVI), *Complejo Hospitalario Universitario de Santiago de Compostela* (CHUS), and *Hospital Clínic Universitari de Valencia*. All the participating institutions are level 1 trauma centres. As we have previously mentioned, three of them (CHUAC, CHUVI and CHUS) are the level 1 trauma centres for the whole region of Galicia, Spain.

The design of the second part of the study and the distribution of patients for the predictive score development are depicted in a flow diagram shown in Figure 30.

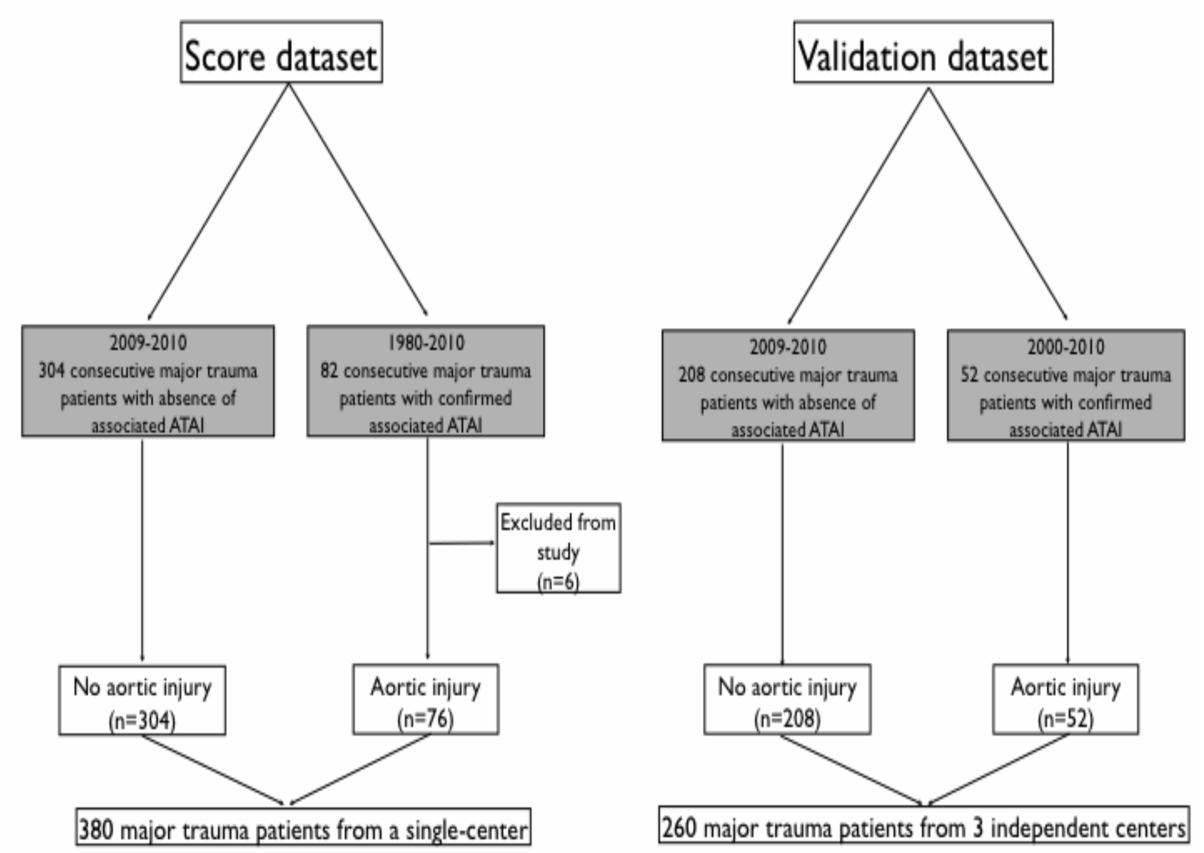


Figure 30. Design of the cross-sectional study for the development of the predictive score and recruitment for both the score and validation datasets.

As we explain in further detail in the next sections (score and validation dataset), it was required to enrol all the consecutive major trauma with ATAI since 1980 from CHUAC to achieve a sufficient number of ATAI cases to develop the score, whereas we only needed to include all the consecutive major trauma patients with ATAI since 2000 from the 3 independent centres to accomplish the score validation. We sought for a proportion of 4 controls (major trauma patients without ATAI) for each case (major trauma with ATAI). Hence, we enrolled the corresponding number of consecutive controls from each of the participating four institutions according to the number of cases provided by each one to reach the aforementioned 4:1 proportion.

4.1.2.1. Score dataset

The score dataset included 82 ATAI patients who were admitted to the CHUAC from January 1980 to December 2010. However, six patients (7.3%) from the ATAI group had to be excluded from the analysis because of insufficient documentation and/or *in extremis* status on arrival.

In order to achieve four control subjects in the NATAI group per patient with ATAI, we selected 304 consecutive patients who presented to our Emergency Department with major trauma with thoracic involvement but without traumatic aortic injury between January 2009 and December 2010. Control subjects were not contemporaneous of cases due to the lack of an institutional codified database for overall major trauma patients before 2006. Identification of cases did not present that drawback thank to the existence of specific databases for ATAIs at both Cardiac Surgery and Radiology Departments.

4.1.2.2. Validation dataset

In the validation dataset, the ATAI group included 52 consecutive major trauma patients with aortic injury who were admitted between January 2000 and December 2010 at the Emergency Departments of the three aforementioned independent collaborating first-level hospitals. Each centre also provided 4 consecutive NATAI major trauma patients per ATAI patient included in the study. A total of 208 consecutive patients with major trauma with thoracic involvement but without aortic injury were included in the validation dataset from the major trauma patients who presented to the emergency departments of the collaborating centres between January 2009 and December 2010. In the validation dataset, no patient was excluded from the analysis because of insufficient documentation and/or *in extremis* status upon arrival.

4.2. Inclusion and exclusion criteria

Inclusion and exclusion criteria were the same for both parts of the research. Recruitment was based on trauma characteristics, it is, blunt major trauma involving chest, and on the results of at least one advanced imaging test that diagnosed or ruled out the presence of an associated traumatic aortic injury. Only adult patients (>15 years-old) were considered for the study.

Patients who were dead on arrival or who died during triage were excluded from the analysis. Penetrating trauma was also an exclusion criterion in this study. All participating centres used the same inclusion/exclusion criteria.

There was not a specific matching process for control patient selection apart from the aforementioned criteria.

All institutions have Institutional Review Board approval to participate in the study, which waived the requirement of written patient consent.

4.3. Imaging data

The ATAI diagnosis was based on imaging (CT, angiography and/or TEE) and, when available, confirmation was provided by surgical visualization and/or autopsy. There was no disagreement in the data provided by the imaging studies.

All participating centres used the same CT acquisition protocols for the trauma patients who required advanced imaging from January 2000.

All of the patients had a portable CXR on admission; either the original taken at the level 1 trauma centre during the initial work-up or a copy of the radiograph that was transferred with the patient from the referring hospital. The admission CXR was obtained in the supine position in 97.9% of the major trauma patients in our study.

Our current institutional CT scan protocol for major trauma with suspected vascular-aortic injury consists of a three-phase MDCT including an unenhanced phase, an arterial contrast-enhanced phase and a delayed phase, with 3D reconstructions. The MDCT is performed using 100-120 ml of intravenous iodinated contrast medium at 4 ml/s in order to maximize arterial enhancement. Axial images are acquired at 0.625 mm collimation during the arterial phase from the thoracic inlet to the symphysis pubis and during the portal venous phase. The images are routinely reviewed in the axial and coronal plane at font images and at a section thickness of 1-3 mm. In vascular MDCT, it is mandatory to generate oblique reconstructions that resemble the images obtained in conventional angiography, as well as sagittal, coronal and MPR [107].

Our MDCT scan protocol varies significantly in major trauma patients with no suspected vascular injury. Axial images are acquired at 1.25 mm collimation during the portal venous phase, after the injection of 60-80 ml of iodinated contrast medium at 2 ml/s.

4.4. Variables collected

Data on 96 variables were recorded on a standardized form including information on patient demographics, mechanism of injury, clinical status on hospital admission (blood pressure, respiratory rate, need of endotracheal intubation at the site of the trauma or during transport, Glasgow Coma Scale [GCS]), Injury Severity Score [292], Abbreviated Injury Score (AIS) for each body area (head, chest, abdomen, extremities), Revised Trauma Score (RTS) [295], Trauma Injury Severity Score (TRISS) [296], head and neck injuries, cardiac injuries, nonmediastinal thoracic injuries, abdominal injuries, pelvic fracture, extremities fractures, findings on admission in simple CXR and performed diagnostic imaging tests (CT, angiography, TEE).

The ISS is an established trauma score that defines the extent of multisystem trauma and expected mortality. The ISS is based upon the AIS of the three most injured body regions of the following: head, face, thorax, abdomen and extremities (pelvis included). The AIS describes the severity of the injury to one body region: 1 minor, 2 moderate, 3 serious, 4 severe, 5 critical, and 6 maximal. In this study, major injury was defined as an AIS > 3. An ISS score of more than 50 points predicts a mortality rate of over 50%, while a score of more than 70 points predicts a mortality rate of nearly 100% [292]. The TRISS score directly predicts the expected death rate for blunt trauma [296].

When present, aortic injury was classified according to its severity as type I (intimal tear), type II (intramural hematoma), type III (pseudoaneurysm) or type IV (rupture) [33, 81], and the site of injury was also recorded (ascending aorta, aortic arch, aortic isthmus and mid and/or distal descending thoracic aorta).

4.5. Definitions

The mechanism of injury was classified as: motor vehicle collision (MVC); motorcycle collision (MCC); auto vs. pedestrian (AVP); fall; crush under weight; and others.

A widened mediastinum was defined on admission CXR as a mediastinal width greater than 8 cm and/or 25% of the width of the thorax [25, 91-93, 100]. The width of the mediastinum was measured at the level of the aortic knob. The chest width indicates the transverse width of the thorax from the inner rib to the inner rib at the level of the aortic knob.

Hemothorax was defined on admission CXR as a blunting of either costophrenic angle due to the accumulation of >250 ml of hematic fluid considered for drainage [297].

Lung contusion was defined in CXR on admission as a characteristic pattern of consolidation not restricted by the anatomical boundaries of the lobes or the segments of the lung [298, 299].

Pelvic fracture-deformity was defined as an unstable pelvis, open pelvic fracture with violated skin overlying the fracture or a suspected pelvic fracture on physical examination (deformity, bruising or swelling over the bony prominences, pubis, perineum or scrotum or leg-length discrepancy or rotational deformity) [300].

Long bong fracture was defined as a proximal long bone fracture suspected by deformity on physical examination.

Left scapula fracture was defined on admission CXR by glenohumeral joint malalignment, angulation of the glenoid neck and fractures of the scapular body, or it was suspected on physical examination by the presence of either deformity, ecchymosis, tenderness and crepitus localized in the area of the left scapula or a “floating shoulder” (when associated with a left clavicle fracture) [301-303].

Hypotension was defined as a systolic blood pressure <90 mmHg or the need of fluid and/or inotropic support to maintain a blood pressure of ≥90 mmHg.

An abnormal respiratory rate was defined as bradypnoea <10 breaths per minute or tachypnoea >30 breaths per minute.

A GCS below 9 points was defined as the cut-off value for a bad neurological prognosis upon admission.

Head injury was defined as a skull fracture, intracranial haematoma, loss of consciousness lasting more than 24 hours, or a parenchymal haemorrhage of the brain.

4.6. Statistical analysis

The data are expressed as the mean and standard deviation or the median and range where appropriate. For bivariate analysis, the proportions were compared with contingency tables by means of chi-square or Fisher’s exact tests, and the Student’s *t* test or Mann-Whitney rank-sum test were used to compare continuous variables.

Relation between the severity of the trauma, defined by the TRISS, RTS and ISS scores, and the different degrees of aortic injury (types I to IV) was tested, using one-way analysis of variance (one-way ANOVA). One-way ANOVA was also used to determine whether there was association between the aortic injury predictive score

(TRAINS) and the degree of severity of the ATAIs. A *P value* of less than 0.05 was considered significant [304].

For the score development, the data analysis consisted of two stages: the determination of easily observable variables and development of the predictive score. In the initial stage, bivariate analysis was used to identify variables with a potential influence on the probability of presenting with an ATAI.

Variables that demonstrated a *P* value <0.10 were entered as independent variables in a stepwise forward binary logistic regression analysis. During modelling, the variables were removed for a *P* value > 0.05, and were entered into the model for a *P* value <0.05 for a maximum of 20 iterations. Thus, stepwise forward binary logistic regression was used to confirm or reject these clinically relevant variables as predictors of aortic injury. The odds ratio (OR), 95% confidence intervals and *P* values were determined. A *P* value of less than 0.05 was selected for variable retention in the final regression model.

The second stage was the development of a prediction score that could be used in the clinical trauma bay of an ER department to determine the probability of aortic injury from clinical and CXR data. We decided that in order to be applicable in the trauma setting, the prediction rule would have to be free of complex calculations.

The relative contribution of each variable to the prediction of ATAI was calculated. Point scores were assigned to each predictive variable confirmed by logistic regression by rounding the corresponding regression beta coefficient to the closest integer value (1 to 4) [305].

The observed and expected rates were compared. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) were calculated in order to determine the performance of the model [306]. While comparing two or more ROC curves based on tests performed on the same set of individuals (observational units), it is also important to account for the correlated nature of the data. The DeLong method is a nonparametric approach to analyse such correlated data based on generalized U-Statistics. The method described by DeLong et al. [307] was used to determine whether there were any statistically significant differences between the AUC directly obtained using the beta coefficients provided by binary logistic regression and the AUC obtained from the score where the beta coefficients were rounded to the closest integer value.

The Hosmer-Lemeshow goodness-of-fit statistic was calculated to assess the calibration of the model [308]. The Hosmer-Lemeshow test assesses whether the observed event rates match expected event rates in subgroups of the model population. The Hosmer-Lemeshow test specifically identified subgroups as the deciles of fitted risk values. We considered the model well calibrated when the expected and observed event rates in the subgroups were similar [309, 310].

The Youden index was calculated to measure the effectiveness of the predictive score and to select an optimal threshold value (cut-off point) for the score [311, 312]. A Chi-square test was also used to determine which score (from 0 to 12 points) achieved the best sensitivity and specificity.

Both positive and negative likelihood ratios were assessed. A likelihood ratio greater than 1 indicated that the test result was associated with the disease. A likelihood ratio less than 1 indicated absence of the disease. Scores with likelihood ratios of close to 1 had little practical significance as this meant that the post-test and pre-test probabilities were similar. When the positive likelihood ratio is greater than 5 or the negative likelihood ratio is less than 0.2 (i.e. 1/5) then a score is considered to be applicable to the pre-test probability of a patient having the disease tested for to estimate a post-test probability of the existing disease state [313].

We performed both an internal and external-multicentre validation of the score. Internal validation of the aortic injury predictive score was accomplished using a simple (no stratified) bootstrap technique. Bootstrap validation is a method of randomly resampling from a given experimental sample to simulate the effect of drawing multiple samples from the same population [291, 314]. Bootstrap analysis was used to formalize the development of the model, removing many of the human biases associated with regression analysis and providing a balance between selecting risk factors that are not reliable (type I error) and overlooking variables that are reliable (type II error), and introducing a concrete measure of the reliability of the risk factors [290]. In the bootstrap procedure 1,000 samples were sampled with replacements from the 380 patients of the score dataset. Enter logistic regression analysis was applied to each bootstrap sample. The stability of the final model was assessed by comparing the frequency of occurrence of the variables of the final model in the bootstrap samples. If the predictors occurred in more than 50% of the bootstrap models they were judged to be reliable and were retained in the final model [290]. Unreliable variables, if present, were removed from the final model.

In the external validation procedure, the same variables identified as predictive variables of ATAIs in the score dataset were evaluated for a possible association with ATAIs in the 260 major trauma patients of the multicentre validation dataset.

The readers of the score were blinded to the results of the standard tests and the patients' diagnoses.

All tests were two-tailed and the SPSS statistical program for Windows version 17.0 (SPSS, Chicago, Illinois) was used to analyse the data.

5. RESULTS

5.1. Results: epidemiology and clinical outcomes of patients with ATAIs among the major blunt chest trauma patients in Galicia between years 2006 to 2010

During the period of 2006-2010, 44 ATAIs were identified among 1,760 major trauma patients (all of them with blunt chest trauma) admitted to public hospitals in Galicia, with an overall percentage of 2.5%. The yearly importance in terms of percentage of ATAIs among the major trauma patients with blunt chest trauma in all Galician public hospitals throughout the study period is shown in Figure 31.

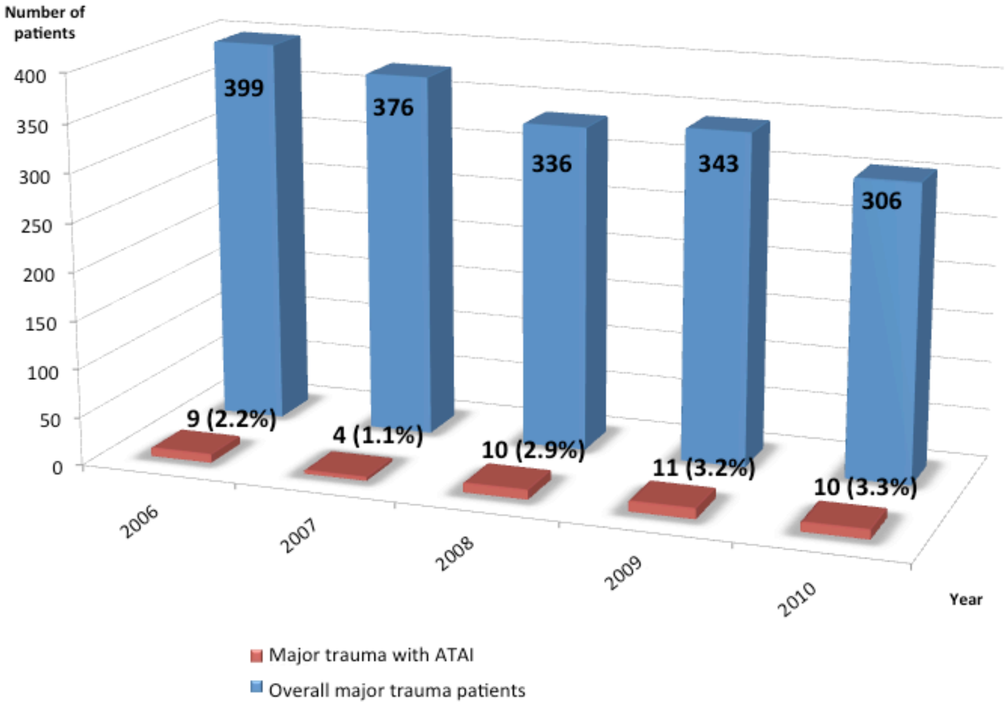


Figure 31. Yearly proportion of ATAI among major trauma patients with blunt chest trauma is depicted for overall Galician public hospitals.

Our institution, CHUAC, admitted 427 major trauma patients with blunt chest trauma during the period of 2006-2010, among which a total of 19 patients (4.4%) with ATAIs were identified (Figure 32).

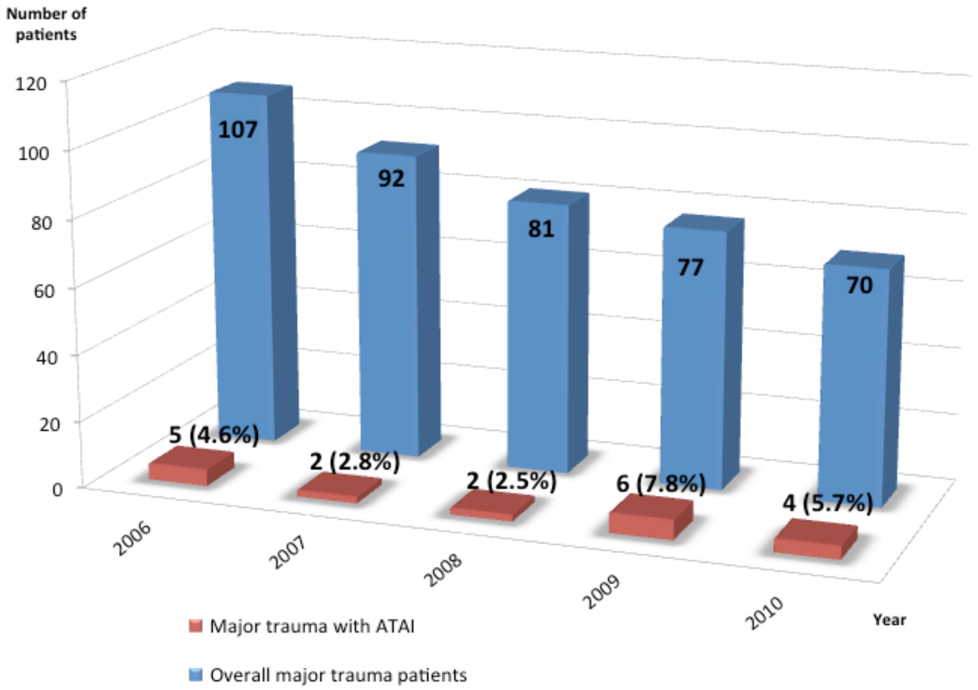


Figure 32. Yearly proportions of ATAIs among the major trauma patients with blunt chest trauma admitted to CHUAC from 2006-2010.

The mean age of overall major trauma patients admitted to a public hospital in Galicia between 2006-2010 was 50.1±20.5 years. Overall, men comprised 77.2% of admissions (1,392 patients), whereas 22.8% were women (412 patients). There were not statistically significant differences in sex distribution between major trauma patients with and without associated ATAI (84.1% of males in ATAI patients vs. 77% in patients without ATAI, *P*=0.27). Nevertheless, major trauma patients with ATAI presented a significantly lower mean age than patients without associated aortic injury (41.2±21 years vs. 50.4±20.5 years, *P*=0.003). The 54.6% of overall ATAIs occurred in major trauma patients between 16 to 35 years old, whereas the age distribution was fairly more homogeneous through the whole age span among major trauma patients without aortic wall injury. Figure 33 depicts the age distribution in the overall major blunt chest trauma patients and in both groups admitted to public hospitals in Galicia between 2006-2010.

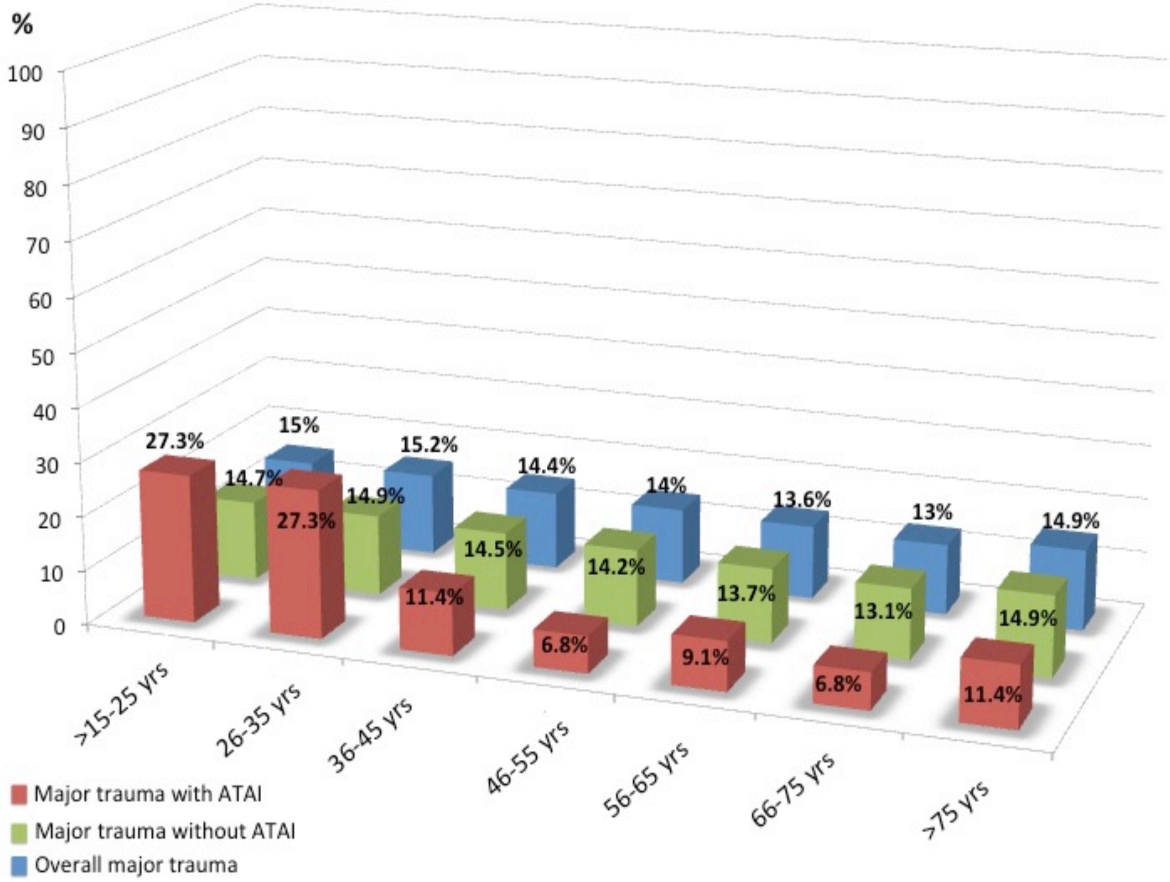


Figure 33. Distribution of age (%) among major overall blunt chest trauma patients (n=1,760 patients), major trauma without ATAI (n=1,716 patients) and major trauma with an associated ATAI (n=44 patients) admitted to public hospitals in Galicia between 2006-2010.

Among the 1,760 major blunt chest trauma patients admitted to public hospitals in Galicia between 2006-2010, the most frequent cause of accident was MVC (850 patients, 48.3%), followed by AVP (487 patients, 27.6%) and falls (199 patients, 11.3%). When comparing major trauma patients with and without associated ATAI, despite MVC was the most common cause of accident in both groups of major trauma patients, MCC (29.5% vs. 8.4%) and crush under weight trauma (11.4% vs. 3.1%) were significantly more frequent among major trauma patients with ATAI, whereas AVP was remarkably more frequent among major trauma patients without aortic wall injury (*P*<0.001) (Figure 34).

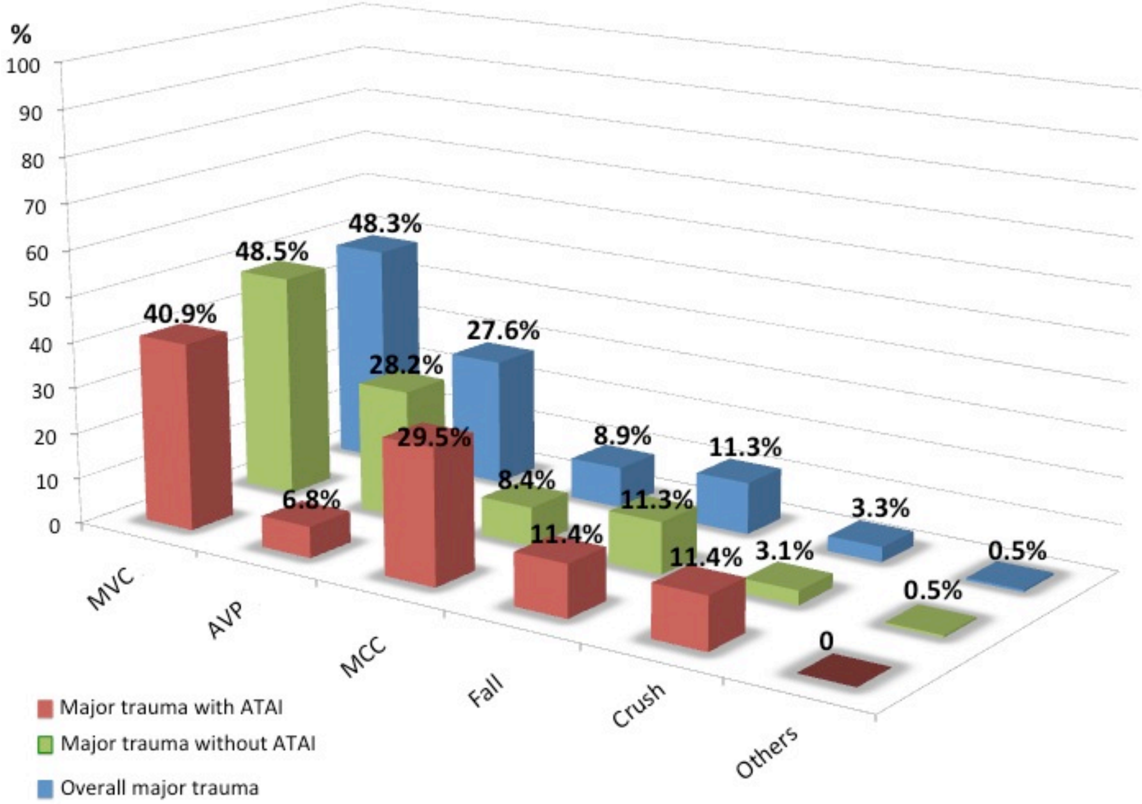


Figure 34. Causes of accident (%) among overall major blunt chest trauma patients (n=1760 patients), major trauma without ATAI (n=1,716 patients) and major trauma with an associated ATAI (n=44 patients) admitted to public hospitals in Galicia between 2006-2010. (MVC= motor vehicle crash; MCC= motorcycle collision; AVP= auto vs. pedestrian).

Mean ISS was 30.2±11.8 for the overall 1,760 major trauma patient. Mean ISS in major trauma patients with ATAI was significantly higher than mean ISS in major trauma patients without aortic wall injury (47.6±18.3 vs. 29.8±11.3, *P*<0.001). A mortality rate over 50% predicted by an ISS score of more than 50 points was found in 177 patients (10.1%) of the overall 1,760 major trauma patients; in 21 patients (47.7%) with ATAI, and in 156 patients (9.1%) without ATAI (*P*<0.001). An ISS score of more than 70 points predicting a mortality rate of nearly 100% was found in 9 patients (20.4%) among major traumas with ATAI, whilst an ISS score >70 was only reached by 3 patients (0.2%) among major trauma patients without aortic injury (*P*<0.001).

The most common site of injury was the isthmus and proximal descending thoracic aorta (56.8%), followed in frequency by the aortic arch (25%) and the mid and distal descending aorta (11.4%) (Figure 35).

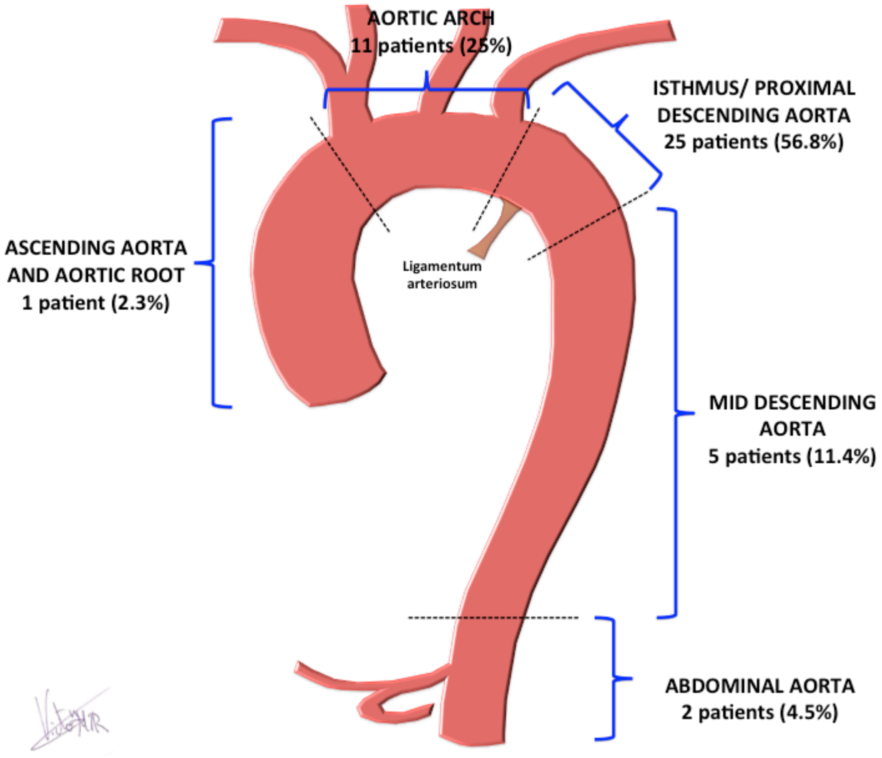


Figure 35. Anatomic location of ATAIs. The graph depicts the anatomic location of the aortic injuries in major trauma patients with an associated ATAI admitted to public hospitals in Galicia between 2006-2010 (n=44 patients).

There were statistically significant differences in the anatomic location of the aortic injury, classified in “isthmal or typical” (isthmus) and “non-isthmal or atypical” (ascending aorta, arch, mid-descending and abdominal aorta), according to the mechanism or cause of injury (*P*=0.046). The isthmus was the most common anatomic site of aortic injury in nearly all the mechanisms of injury, except for the crush under weight. Indeed, ATAIs caused by falls presented a “typical” location at the aortic isthmus in all the cases.

The anatomic distribution of ATAIs slightly differed between motor-vehicle related accidents (MVCs and MCCs) and other blunt trauma cases, outstanding the higher frequency of injuries in the aortic arch (32.3% arch injuries in motor-vehicle accidents vs. 7.7% arch injuries in other mechanisms of ATAI; *P*=0.18). Regarding crush or non-decelerating trauma, “non-isthmal or atypical” injuries were more common than in decelerating or high-speed causes of trauma (80% atypical in crush vs. 38.5% in decelerating traumas; *P*=0.07).

The frequencies of anatomic location of ATAIs according to the mechanism of injury are summarized in Table 11.

Anatomic location	**Mechanism of injury**	**MVC n (%)**	**AVP n (%)**	**MCC n (%)**	**Fall n (%)**	**Crush n (%)**	***P-value***
Isthmus injury		9 (50%)	2 (66.7%)	8 (61.5%)	5 (100%)	1 (20%)	0.046
“Non-isthmal or atypical” injuries		9 (50%)	1 (33.3%)	5 (38.5%)	0	4 (80%)	

TABLE 11. Anatomic location of the ATAIs vs. mechanisms of the aortic injury. The distribution of the anatomic location of ATAIs, which was classified in “isthmal or typical” and “non-isthmal or atypical” aortic injuries, is compared among the different mechanisms of injury. (MVC= motor vehicle crash; MCC= motorcycle collision; AVP= auto vs.

pedestrian).

According to the international classification for severity of traumatic aortic injuries, the 44 major trauma patients with an associated ATAI admitted to public hospitals in Galicia between 2006-2010 presented 11.4% type I (intimal tear), 15.9% type II (intramural hematoma), 29.5% type III (pseudoaneurysm), and 43.2% type IV (rupture) traumatic aortic injuries. A 72.7% of patients presented high-risk aortic injuries (type III and type IV), whereas a low-risk aortic injury (type I and type II) appeared in 27.3% of patients.

Statistically significant differences in the severity of ATAIs, classified in low-degree (types I-II) and high-degree (types III-IV) injuries, were found among the different mechanism of injury involved in the major trauma (*P*=0.045). Crush trauma patients presented significantly more frequent low-risk aortic injuries than other mechanism of injury (80% vs. 20.5%; *P*=0.023). On the contrary, MCC traumas presented a dramatically higher frequency of high-degree aortic injuries. The severity of ATAIs according to the mechanism of injury is summarized in Table 12.

Severity of ATAI	**Mechanism of injury**	**MVC n (%)**	**AVP n (%)**	**MCC n (%)**	**Fall n (%)**	**Crush n (%)**	***P-value***
Low-degree injuries (types I and II)		5 (27.8%)	1 (33.3%)	1 (7.7%)	1 (20%)	4 (80%)	0.045
High-degree injuries (types III and IV)		13 (72.2%)	2 (66.7%)	12 (92.3%)	4 (80%)	1 (20%)	

TABLE 12. **Severity of the ATAIs vs. mechanisms of the aortic injury.** The distribution of the severity of ATAIs, which was classified in low-degree (types I-II) and high-degree (types III-IV) injuries, is compared among the different mechanisms of

injury. (MVC= motor vehicle crash; MCC= motorcycle collision; AVP= auto vs. pedestrian).

There were also statistically significant differences in the severity of ATAIs among the distinct anatomic locations of the ATAIs (*P*=0.04). The severity of ATAIs according to their anatomic location is presented in Table 13.

Severity of ATAI	**Anatomic location**	**Ascending aorta n (%)**	**Arch n (%)**	**Isthmus n (%)**	**Mid-descending aorta n (%)**	**Abdominal aorta n (%)**	***P-value***
Low-degree injuries (types I and II)		0	3 (27.3%)	4 (16%)	3 (60%)	2 (100%)	0.04
High-degree injuries (types III and IV)		1 (100%)	8 (72.7%)	21 (84%)	2 (40%)	0	

TABLE 13. **Severity of the ATAIs vs. anatomic location of the ATAIs.** The distribution of the severity of ATAIs, which was classified in low-degree (types I-II) and high-degree (types III-IV) injuries, is compared among the distinct possible anatomic locations of ATAIs.

Overall in-hospital mortality was 10.2% (180 patients) among the 1,760 major blunt chest trauma patients admitted to public hospitals in Galicia between 2006-2010, whereas trauma patients with ATAI presented a significantly higher in-hospital mortality (17 patients, 38.6%) than those trauma patients without ATAI (163 patients, 9.5%) (*P*<0.001). Additionally, in-hospital mortality tended to be different among the distinct anatomic locations of the ATAIs, although this difference did not reach statistically significance (*P*=0.13). Ascending aorta and arch injuries presented both an in-hospital mortality over 50% (100% and 63.6%, respectively), whereas none of the other anatomic locations had an in-hospital mortality over 40% (isthmus, 28%; mid-descending aorta, 40%; and no mortality in abdominal aortic injuries). In fact, differences in in-hospital mortality were close to reach statistical significance when comparing injuries at isthmus with “atypical or non-isthmal” aortic injuries (41.2% vs. 58.8%; *P*=0.08).

The median in-hospital stay length for the overall 1,760 major blunt chest trauma patients admitted to public hospitals in Galicia between 2006-2010 was 20 days (range 0 to 875 days). In the subset of trauma patients with ATAI, the median in-hospital stay length was 18 days (range 0 to 115 days), and 20 days (range 0 to 875 days) in major trauma patients without aortic injury (*P*=0.24).

5.2. Results: predictive scoring method

5.2.1. Description of the score dataset

As we mentioned previously in the chapter *Patients and Methods*, the score dataset included 380 major trauma patients (76 patients with ATAIs and 304 patients without aortic injury). In the overall score dataset (ATAI and NATAI patients), most of the patients were male (84.7%) with a mean age of 43.16 ± 18.27 years, including 28.7% of the patients who were over 55 years. The expected mortality at admission was ≥50% according to an ISS score >50 points in 11.5% of the patients, while the overall mean expected death rate according to the TRISS score was 22.44 ± 28.63%. All patients had at least one severe extrathoracic injury with AIS >3. Clinical and radiological data were available for all patients in both groups (ATAI and NATAI) and are presented in Table 10.

Variable	**ATAI group**	**NATAI group**	***p*-value**
Sex (male)	82.9%	85.2%	0.61
Age	41.33±18.14	43.62±18.30	0.32
Age ≥55 years	26.3%	29.3%	0.61
Mechanism of injury			0.002
MVC	61.8%	39.2%	
MCC	14.5%	14.8%	
Fall	10.5%	26%	
AVP	6.6%	11.5%	
Crush under weight	6.6%º <	8.5%	

Diagnostic tests on admission			
CT scan	68.4%	91.7%	<0.001
Angiography	42.1%	12.2%	<0.001
TEE	63.1%	26.9%	<0.001
ISS	40.45±14.32	29.95±11.03	<0.001
RTS	5.98±1.71	6.97±1.34	<0.001
TRISS (%)	38.06±36.44	18.54±24.91	<0.001

Table 14. Epidemiological, clinical and diagnostic characteristics of the patients of the score dataset. The *P* value of the proportions analysis was obtained with the χ^2 test, while the *P* value mean analysis corresponds to Student's *t* test (ATAI group = acute traumatic aortic injury; NATAI group =no associated acute traumatic aortic injury; MVC= motor vehicle crash; MCC= motorcycle collision; AVP= auto vs. pedestrian; CT= computed tomography; TEE= transesophageal echocardiography; ISS= Injury Severity Score; AIS= Abbreviated Injury Score; RTS= Revised Trauma Score; TRISS= Trauma Injury Severity Score).

The locations of the aortic injury in the score dataset were: aortic isthmus, 64.5%; mid-distal descending aorta, 15.8%; aortic arch, 11.9%; ascending aorta, 3.9%; and peridiaphragmatic aorta, 3.9%.

According to the international classification for traumatic aortic injuries, the 76 ATAI patients included in the score dataset presented 25% type I (intimal tear), 22.4% type II (intramural hematoma), 22.4% type III (pseudoaneurysm), and 30.2% type IV (rupture) traumatic aortic injuries. The one-way ANOVA revealed that there was no relation between the severity of the trauma defined by the TRISS (*P*=0.77), the ISS (*P*=0.59) or the RTS (*P*=0.73) scores and the severity of aortic injury (types I to IV).

Overall in-hospital mortality was 11.8%, whereas in-hospital mortality was 26.3% in ATAI group, and 8.2% in NATAI group. There was a significantly higher in-hospital mortality in the group of patients with ATAI (*P*<0.001). Causes of death are summarized in Table 15.

Cause of death	**Deaths in ATAI group N=20 (%)**	**Deaths in NATAI group N=25 (%)**	**Chi-square**
Hypovolemic shock	7 (35%)	3 (12%)	<0.001
Neurologic- brain herniation	3 (15%)	7 (28%)	
Multisystem organ failure	5 (25%)	8 (32%)	
Septic shock	2 (10%)	4 (16%)	
Respiratory-ARDS	1 (5%)	3 (12%)	
Cardiogenic shock or cardiac tamponade	2 (10%)	0	

Table 15. Distribution of the causes of in-hospital mortality in the score dataset.

(ADRS=Acute respiratory distress syndrome).

There were no statistically significant differences in the length of ICU and hospital stays between the two groups of major trauma patients. The overall median length of ICU stay was 10 days (range 0 to 448 days), whilst the median length of ICU stay in the ATAI group was 16 days (range 0 to 123 days), with 9 days (range 0 to 448 days) in the NATAI group (*P*=0.11). The overall median length of the stay in hospital was 26 days (range 0 to 587 days). In the ATAI group, the median length of the stay in hospital was 30 days (range 0 to 547 days), with 25 days (range 0 to 587 days) in the NATAI group (*P*=0.79).

5.2.2. Development of the predictive score

In the first step, bivariate analysis suggested 18 variables having a potential influence on the probability of the major trauma patients in the score dataset presenting with an aortic injury (Table 16). Other 11 different analysed variables were not statistically significant in bivariate analysis (Table 16).

Variable	ATAI group	NATAI group	*P*-value
First rib fracture	17.1%	8.2%	0.021
Left ribs fracture	69.7%	47%	<0.001
Right ribs fracture	31.6%	43.4%	0.061
Sternal fracture	9.2%	5.9%	0.301
Left clavicle fracture	11.8%	8.6%	0.375
Right clavicle fracture	2.6%	4.9%	0.385
Left scapula fracture	28.9%	7.9%	<0.001
Right scapula fracture	2.6%	5.6%	0.290
Pelvic fracture	51.3%	15.5%	<0.001
Long bone fracture	21.1%	4.6%	<0.001
Head injury	21.1%	18.7%	0.61
Spine fracture	24.3%	23.7%	0.905
Lung contusion	93.4%	59.9%	<0.001
Diaphragmatic rupture	9.2%	2.3%	0.004
Cardiac injury	23.7%	5.6%	<0.001
Liver injury	27.6%	16.4%	0.025

Spleen injury	21.1%	14.5%	0.159
Bowel injury	10.5%	5.3%	0.092
Kidney injury	18.4%	7.9%	0.006
Bladder injury	3.9%	0.7%	0.024
Hemoperitoneum	43.4%	17.8%	<0.001
Pneumoperitoneum	1.3%	3.3%	0.359
Hemothorax	77.6%	44.7%	<0.001
Pneumothorax	38.2%	39.5%	0.834
Widened mediastinum	78.9%	24%	<0.001
Hypotension <90 mmHg	76.3%	19.1%	<0.001
Altered respiratory rate	59.2%	30.6%	<0.001
Need of ETI	65.8%	32.2%	<0.001
GCS <9	34.2%	21.7%	0.023

Table 16. Results of the bivariate analysis for the patients of the score dataset. (ATAI group = acute traumatic aortic injury; NATAI group= no associated acute traumatic aortic injury; ETI= endotracheal intubation; GCS= Glasgow Coma Score).

We confirmed that the diagnostic accuracy on admission CXR of a widened mediastinum, tested as a single predictive sign, was limited with a sensitivity of 78.9% and a specificity of 75.9%.

Subsequently, of the 18 potentially influence variables suggested by the bivariate analysis, the stepwise forward binary logistic regression only confirmed widened mediastinum, hypotension, hemothorax, lung contusion, left scapula fracture, pelvic fracture-deformity and long bone fracture on admission as risk factors for the presence of an associated traumatic aortic injury in major trauma patients (Table 17). These variables were assigned a score between 1 and 4 points according to their corresponding beta coefficient provided by stepwise forward logistic regression, which was rounded to the closest integer value (1 to 4), as shown in Table 17. Thus, the scoring method obtained could rank from 0 to 12 points.

Variable	Beta coefficient	OR	95% CI for OR	*P-value*	Score
Widened mediastinum	3.42	30.82	12.05-78.81	<0.001	4
Hypotension <90 mmHg	1.76	5.85	2.26-15.15	<0.001	2
Long bone fracture	2.15	8.60	2.15-34.31	0.002	2
Lung contusion	1.41	4.12	1.11-15.20	0.033	1
Left scapula fracture	1.34	3.81	1.24-11.69	0.019	1
Hemothorax	1.24	3.47	1.19-10.09	0.023	1
Pelvic fracture-deformity	1.08	2.96	1.15-7.60	0.024	1

Table 17. Results of the binary stepwise forward logistic regression and the corresponding score assigned to each significant variable according to its OR. (OR= Odds ratio; CI= Confidence Interval).

The ROC curve corresponding to the aforementioned score (TRAINS) presented an area under the curve of 0.96 (0.95-0.98) (Figure 36).

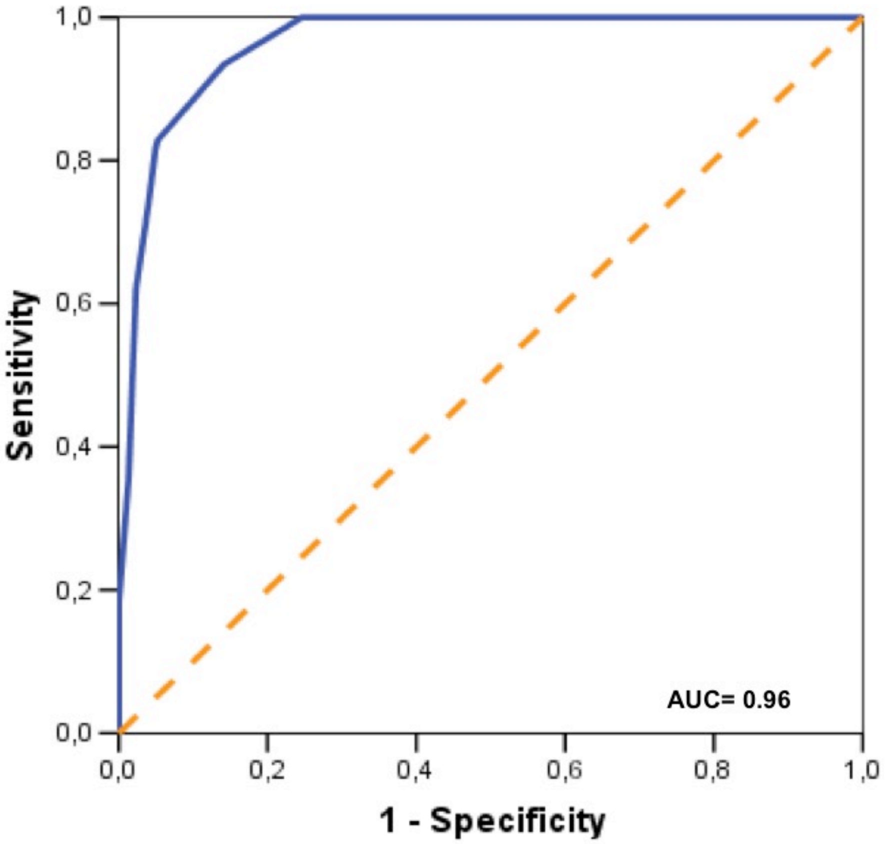
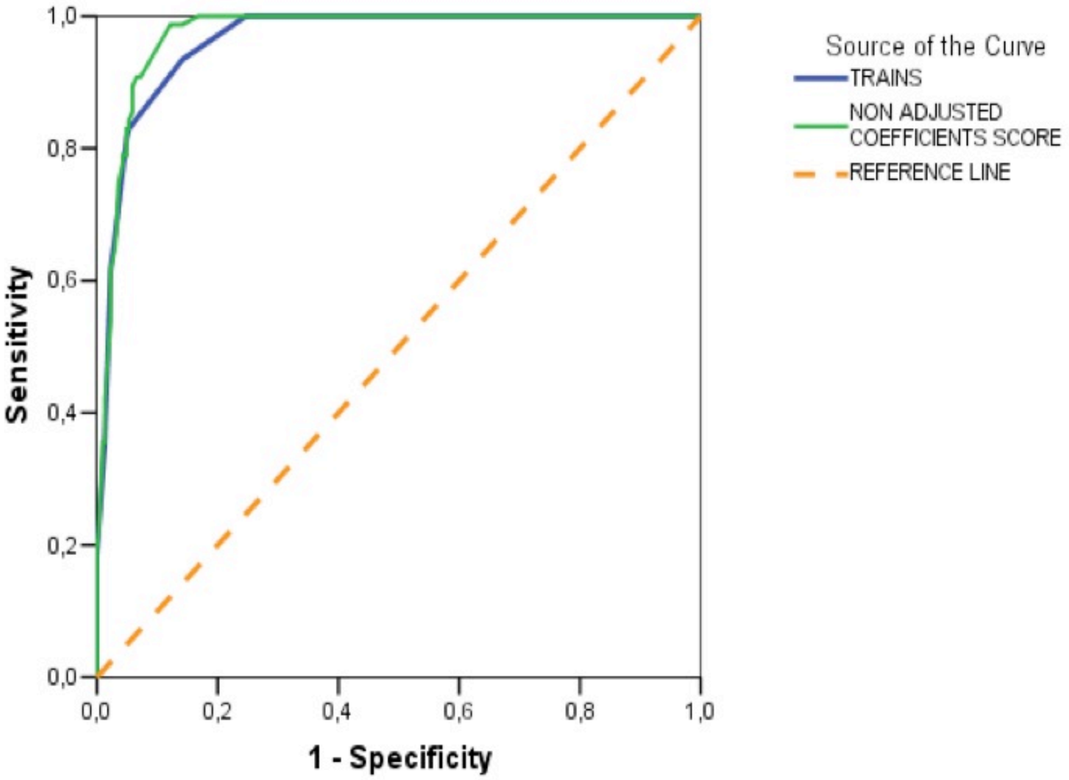


Figure 36. ROC curve of the TRAINS in the score dataset. The ROC curve obtained using the TRAINS in the score dataset presented an area under the curve (AUC) of 0.96 (0.95-0.98).

The ROC curve for the score constructed using directly the non-rounded or original beta coefficients was also calculated. This ROC curve for the non-adjusted coefficient score had an AUC of 0.97 (0.96-0.99).

Using the DeLong method, no statistically significant differences were found between the ROC curves (with and without beta coefficients rounded to the closest integer number) (Chi-square value=2.21; *P*=0.14) (Figure 37).



ROC CURVE	AUC	CI 95%	S.E. (DeLong)
TRAINS	0.96	0.95-0.98	0.009
Non-rounded Score	0.97	0.96-0.99	0.007

Figure 37. DeLong method for ROC curves comparison. The graph shows the comparison using the DeLong method between both AUC and ROC curves obtained in the score dataset, one of them with original beta coefficients (green curve) and the other with beta coefficients rounded to the closest integer value (blue curve). (ROC= receiver operating characteristic; AUC= area under the curve; CI= confidence interval).

The Hosmer-Lemeshow goodness-of-fit statistic across the groups of risk was not statistically significant (Chi square value= 13.14, *P*=0.10; Table 18), indicating little departure from a perfect fit.

		No aortic injury		**Aortic injury**		Total
		Observed	**Expected**	**Observed**	**Expected**	
Step	1	49	48.90	0	0.09	49
	2	33	32.78	0	0.22	33
	3	68	67.44	0	0.55	68
	4	27	26.50	0	0.49	27
	5	49	47.63	0	1.36	49
	6	38	36.46	1	2.53	39
	7	25	31.21	13	6,79	38
	8	11	11.16	30	29.83	41
	9	4	1.90	32	34.09	36

Table 18. Results of the Hosmer-Lemeshow goodness-of-fit test in the score dataset.

A score of ≥4 points was defined as the threshold value for maximum sensitivity and specificity. It provided a sensitivity of 93.42% (87.19%-99.65%) and a specificity of 85.85% (81.77%-89.94%). Youden's index for a score ≥4 was 0.79 (0.72-0.86), while the positive likelihood ratio was 6.60 (4.98-8.77) and the negative likelihood ratio was 0.08 (0.03-0.18).

Other cut-off values tested were a score ≥3 points, which provided a sensitivity of 97.2% (95.2%-100%) and a specificity of 53% (47.34%-58.65%), and a score ≥5 points, which involved a sensitivity of 74.68% (64.46%-84.9%) and a specificity of 94.74% (92.06%-97.41%).

Figure 38 shows the distribution of the score dataset patients according to the TRAINS results obtained using a cut-off value of ≥4 points. As can be seen in the diagram, the five ATAI patients with a TRAINS <4 (false negatives) presented low-risk aortic injuries, which were either small intimal tears or intramural haematomas without intimal tears.

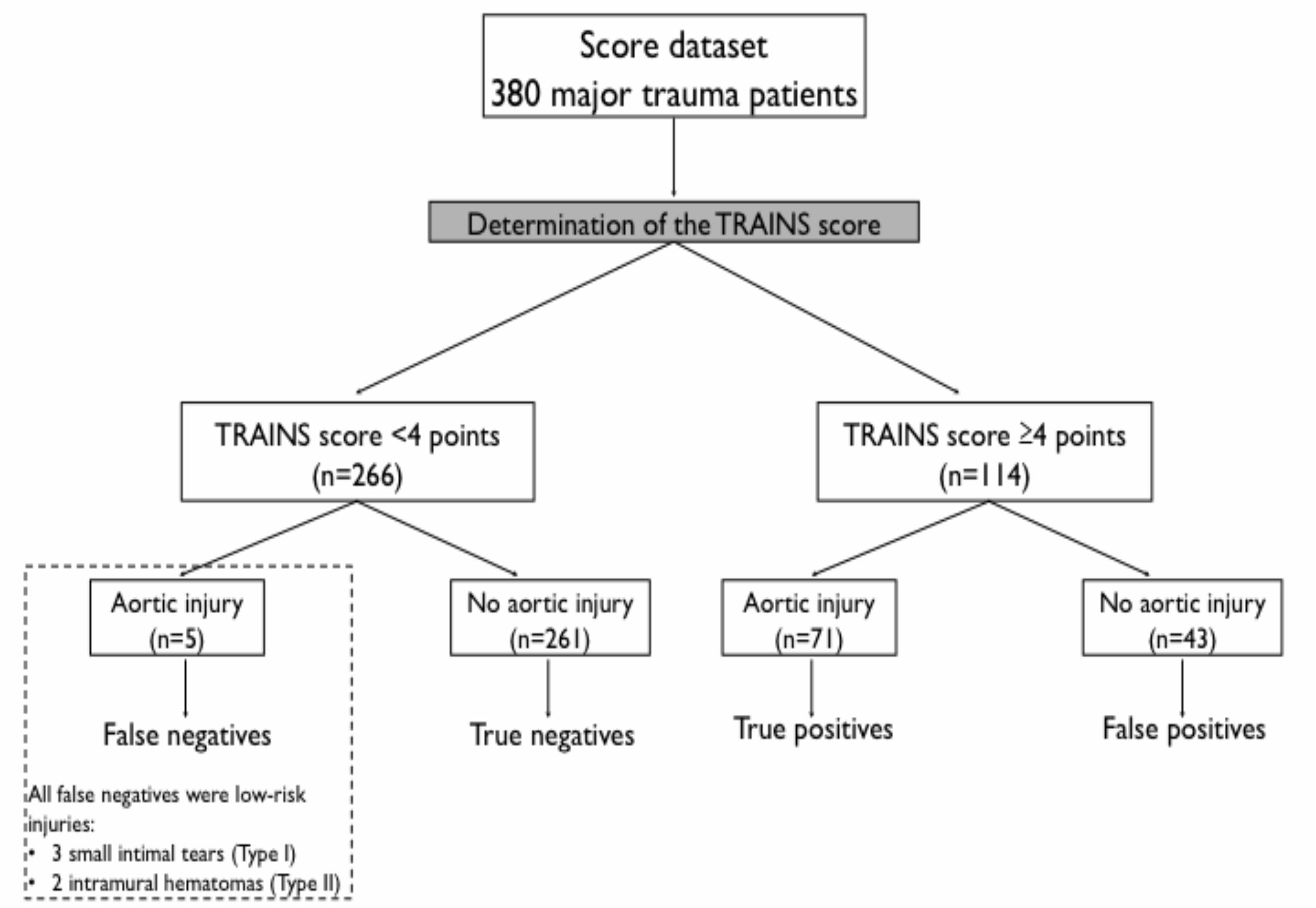
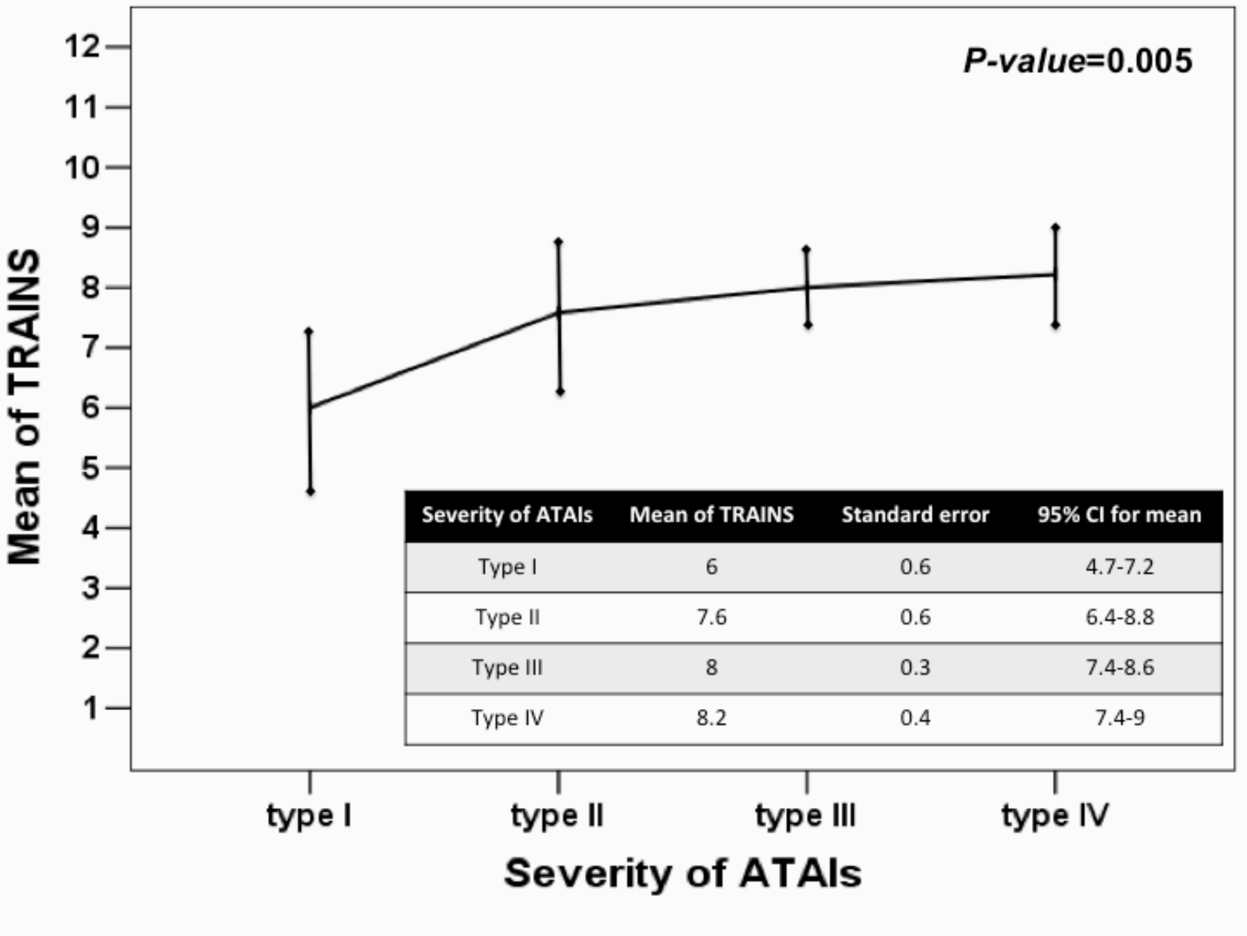


Figure 38. Distribution of patients from the score dataset according to their TRAINS result.

Moreover, the one-way ANOVA demonstrated that there was a significant relationship between the TRAINS score and the severity of aortic injury (types I to IV) (p=0.005), as we may observe in Figure 39.



Severity of ATAIs	Mean of TRAINS	Standard error	95% CI for mean
Type I	6	0.6	4.7-7.2
Type II	7.6	0.6	6.4-8.8
Type III	8	0.3	7.4-8.6
Type IV	8.2	0.4	7.4-9

Figure 39. Means of TRAINS results among the different degrees of severity of the aortic injuries in the score dataset (CI= confidence interval).

In contrast, the one-way ANOVA demonstrated that the severity of the trauma defined by the classical trauma scores (TRISS, ISS and RTS) have no statistically significant relationship with the severity of the aortic injuries (types I to IV). These relationships are shown in Figure 40.

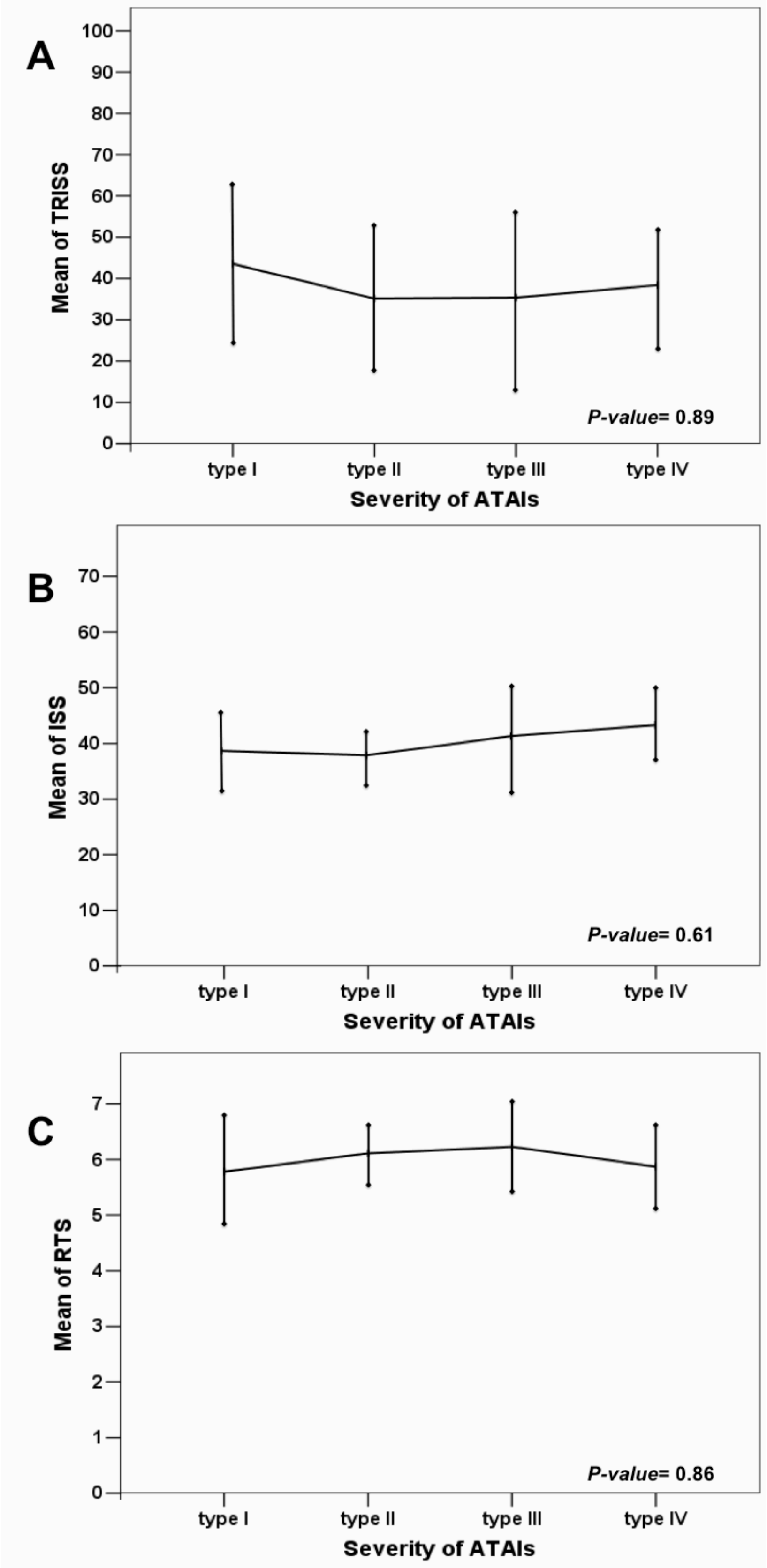


Figure 40. Means of trauma scores, TRISS (A), ISS (B) and RTS (C), among the different degrees of severity of the aortic injuries in the score dataset (CI= confidence interval).

5.2.3. Description of the validation dataset

As we have previously mentioned in the chapter *Patients and Methods*, the validation dataset included 260 major trauma patients from three independent first-level trauma centres (52 patients with ATAIs and 208 patients without aortic injury). In the overall validation dataset (ATAI and NATAI patients), most of patients were male (74.2%) with a mean age of 45.5 ± 19.54 years, including 32.7% of the patients who were over 55 years. The expected mortality at admission was ≥50% according to an ISS score >50 points in 16.4% of the patients, while the overall mean expected death rate according to the TRISS score was 24.21 ± 30.52%. All patients had at least one severe extrathoracic injury with AIS>3. The data for the patients of the validation dataset are shown in Table 19.

Variable	**ATAI group**	**NATAI group**	***P*-value**
Sex (male)	78.8%	73.1%	0.395
Age	37.35±18.13	47.54±19.39	<0.001
Age ≥55 years	15.4%	37%	0.003
Mechanism of injury			0.013
MVC	50%	36.5%	
MCC	23.1%	13%	
Fall	11.5%	33.7%	
AVP	5.8%	7.2%	
Crush under weight	5.8%	7.7%	
Others	3.8%	1.9%	

Diagnostic tests on admission			
CT scan	94.4%	93.7%	0.9
Angiography	30.7%	6.7%	<0.001
TEE	57.7%	16.3%	<0.001
ISS	38.67±18.29	31.85±14.47	0.004
RTS	6.22±1.81	7.02±1.33	<0.001
TRISS (%)	31.46±34.63	21.39±29.21	0.055

Table 19. Epidemiological, clinical and diagnostic characteristics of the patients of the validation dataset. The *P* value of the proportions analysis was obtained with the χ^2 test, while the *P* value for the mean analysis was obtained with the Student's *t* test. (ATAI group = acute traumatic aortic injury; NATAI group =no associated acute traumatic aortic injury; MVC= motor vehicle crash; MCC= motorcycle collision; AVP= auto vs. pedestrian; CT= computed tomography; TEE= transesophageal echocardiography; ISS= Injury Severity Score; AIS= Abbreviated Injury Score; RTS= Revised Trauma Score; TRISS= Trauma Injury Severity Score).

The locations of the aortic injuries in the validation dataset were: aortic isthmus, 55.8%; mid-distal descending aorta, 23.1%; aortic arch, 19.2%; and ascending aorta, 1.9%.

According to the international classification for traumatic aortic injuries, the 52 ATAI patients included in the validation dataset presented 15.4% type I, 15.4% type II, 28.8% type III, and 40.4% type IV traumatic aortic injuries

Overall in-hospital mortality in the validation cohort was 15%, whilst in-hospital mortality was 34.6% in ATAI group, and 10.1% in NATAI group. There was a significantly higher in-hospital mortality in the group of patients with ATAIs (*P*<0.001). The causes of death in the validation dataset are summarized in Table 20.

Cause of death	**Deaths in the ATAI group N=18 (%)**	**Deaths in the NATAI group N=21 (%)**	**Chi-square**
Hypovolemic shock	11 (61.1%)	4 (19%)	<0.001
Neurologic- Brain herniation	2 (11.1%)	7 (33.4%)	
Multisystem organ failure	4 (22.2%)	5 (23.8%)	
Septic shock	1 (5.6%)	2 (9.5%)	
Respiratory-ARDS	0	3 (14.3%)	
Cardiogenic shock or cardiac tamponade	0	0	

Table 20. Distribution of the causes of in-hospital mortality in the validation dataset (ADRS=Acute respiratory distress syndrome).

No statistically significant differences in the length of the ICU and hospital stays were found between the two groups of major trauma patients. The overall median length of ICU stay was 6 days (range 0 to 157 days), whilst the median length of ICU stay for the ATAI group was 5 days (range 0 to 64 days), with 18 days (range 0 to 142 days) for the NATAI group (*P*=0.11). The overall median length of the stay in hospital was 19 days (range 0 to 449 days). In the ATAI group, the median length of the stay in hospital was 30 days (range 0 to 547 days), with 25 days (range 0 to 587 days) for the NATAI group (*P*=0.79).

5.2.4. Validation of the predictive score

5.2.4.1. Internal validation

The internal validation was performed using a simple (non-stratified) bootstrap method and 1,000 samples from the 380 major trauma patients of the score dataset. The bootstrap results for the variables included in the binary logistic regression are shown in Table 21.

Variable	Beta coefficient	Bias	Standard error	*P-value* (2-tailed)	95% CI for the beta coefficient
Widened mediastinum	3.42	0.29	1.32	0.001	2.49-5.15
Hypotension <90 mmHg	1.76	0.15	0.86	0.001	0.72-3.18
Long bone fracture	2.15	0.16	1.02	0.001	0.62-3.95
Lung contusion	1.41	0.26	1.41	0.011	0.37-3.09
Left scapula fracture	1.34	0.12	0.92	0.023	0.038-278
Hemothorax	1.24	0.07	0.61	0.017	0.19-2.67
Pelvic fracture-deformity	1.08	0.02	0.79	0.028	0.20-2.24

Table 21. Bootstrap results for the variables included in the equation (CI= confidence interval).

5.2.4.2. External validation

Applying the TRAINS model to the validation dataset of 260 major trauma cases revealed an ROC curve of 0.93 (0.89-0.98) (Figure 41). The DeLong method demonstrated that the validation dataset ROC curve was similar to the ROC curve for the score dataset, indicating a good discriminatory power (Chi-square value=2.11; *P*=0.11).

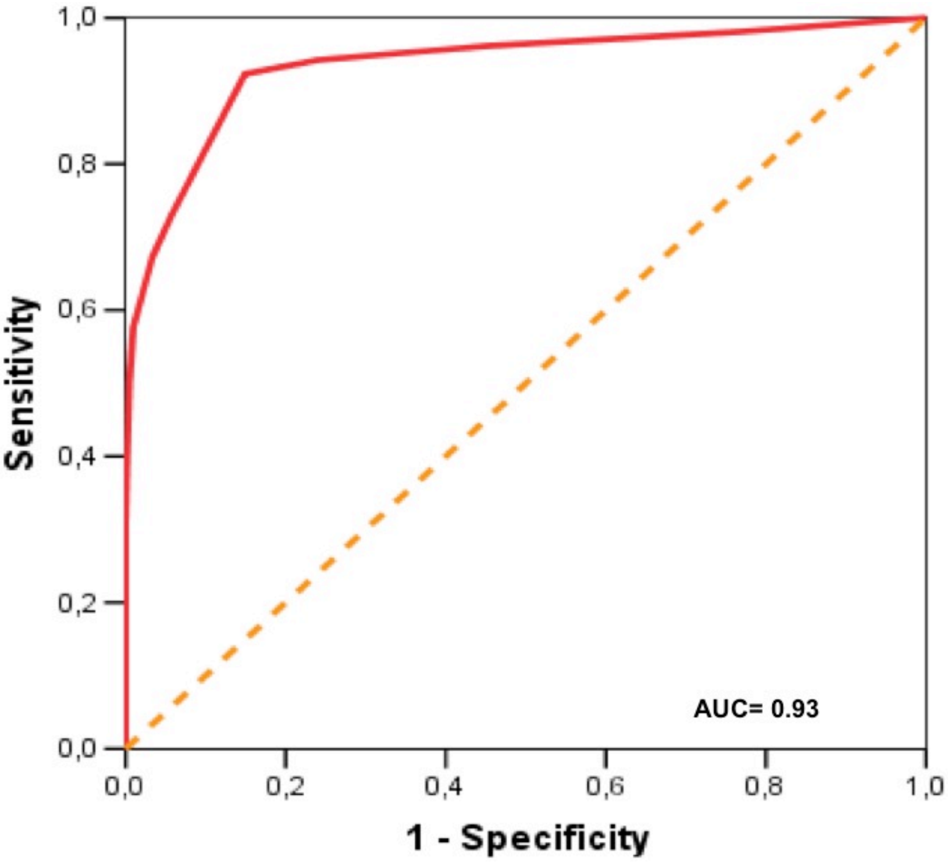


Figure 41. ROC curve of TRAINS in validation dataset. The ROC curve obtained by using the TRAINS in the validation dataset presented an area under the curve (AUC) of 0.93 (0.89-0.98).

The Hosmer-Lemeshow test was not statistically significant (Chi-square= 2.17; *P*=0.9. Table 22), revealing little departure from a perfect fit.

		No aortic injury		**Aortic injury**		Total
		Observed	**Expected**	**Observed**	**Expected**	
Step	1	36	35.7	0	0.29	36
	2	49	49.5	0	0.49	49
	3	26	25.6	0	0.39	26
	4	32	32.45	1	1.55	33
	5	26	25.36	1	1.63	27
	6	23	24.36	5	4.64	28
	7	14	14.01	10	8.64	24
	8	1	1.01	15	14.01	16
	9	1	0.16	20	19.99	21

Table 22. Results of the Hosmer-Lemeshow goodness-of-fit test in the validation dataset.

In the validation dataset the score demonstrated a sensitivity of 92.31% (86.1%-100%) and a specificity of 85.1% (80.02%-90.18%). The Youden's Index for a score ≥4 was 0.77 (0.69-0.86), while the positive likelihood ratio was 6.19 (4.43-8.65) and the negative likelihood ratio was 0.09 (0.04-0.23). Figure 42 shows the distribution of the score dataset patients according to the TRAINS result obtained. As can be seen in the diagram, the four ATAI patients with a TRAINS <4 (false negatives) presented low-risk aortic injuries, which were either small intimal tears or intramural haematomas without intimal tear.

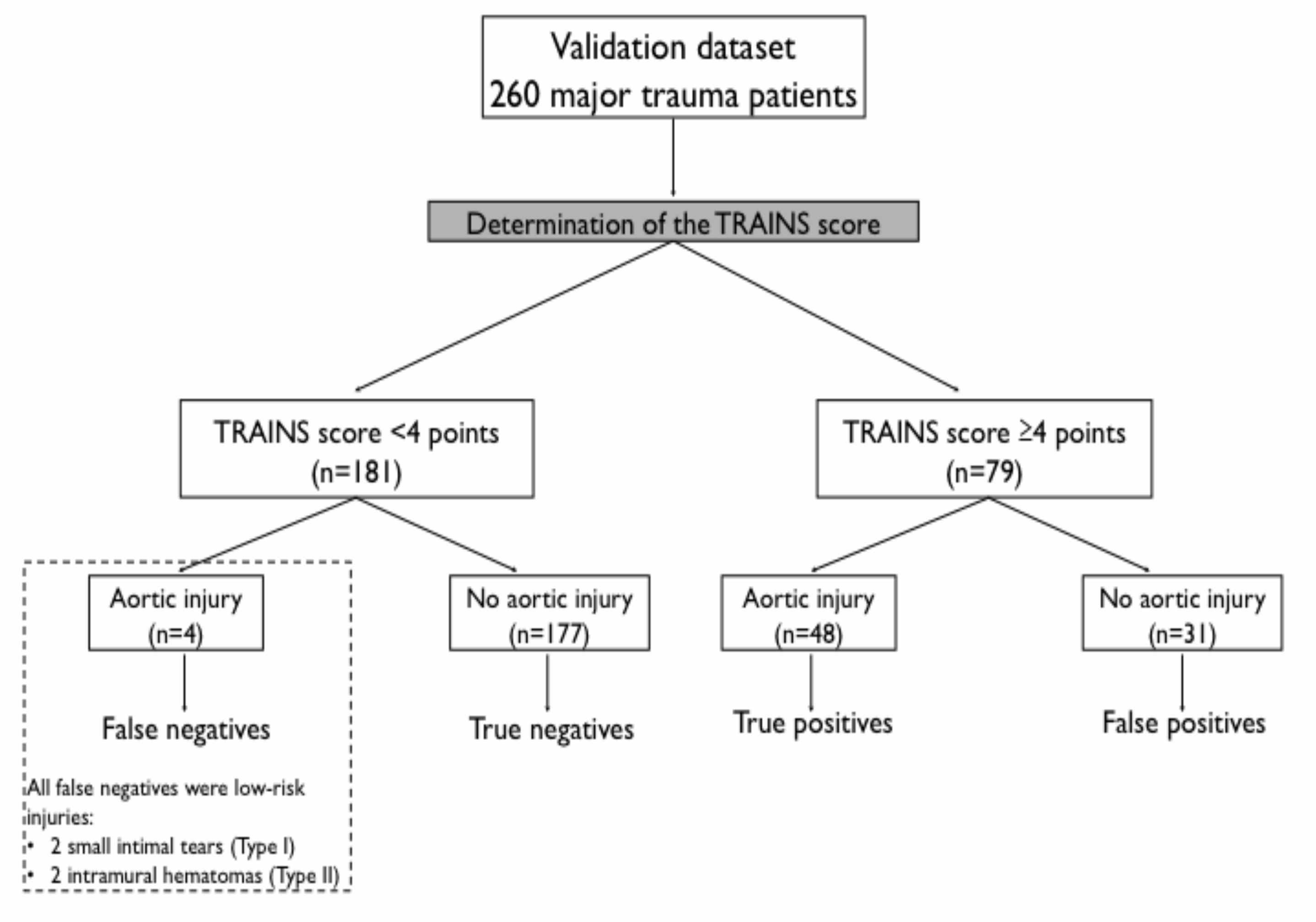
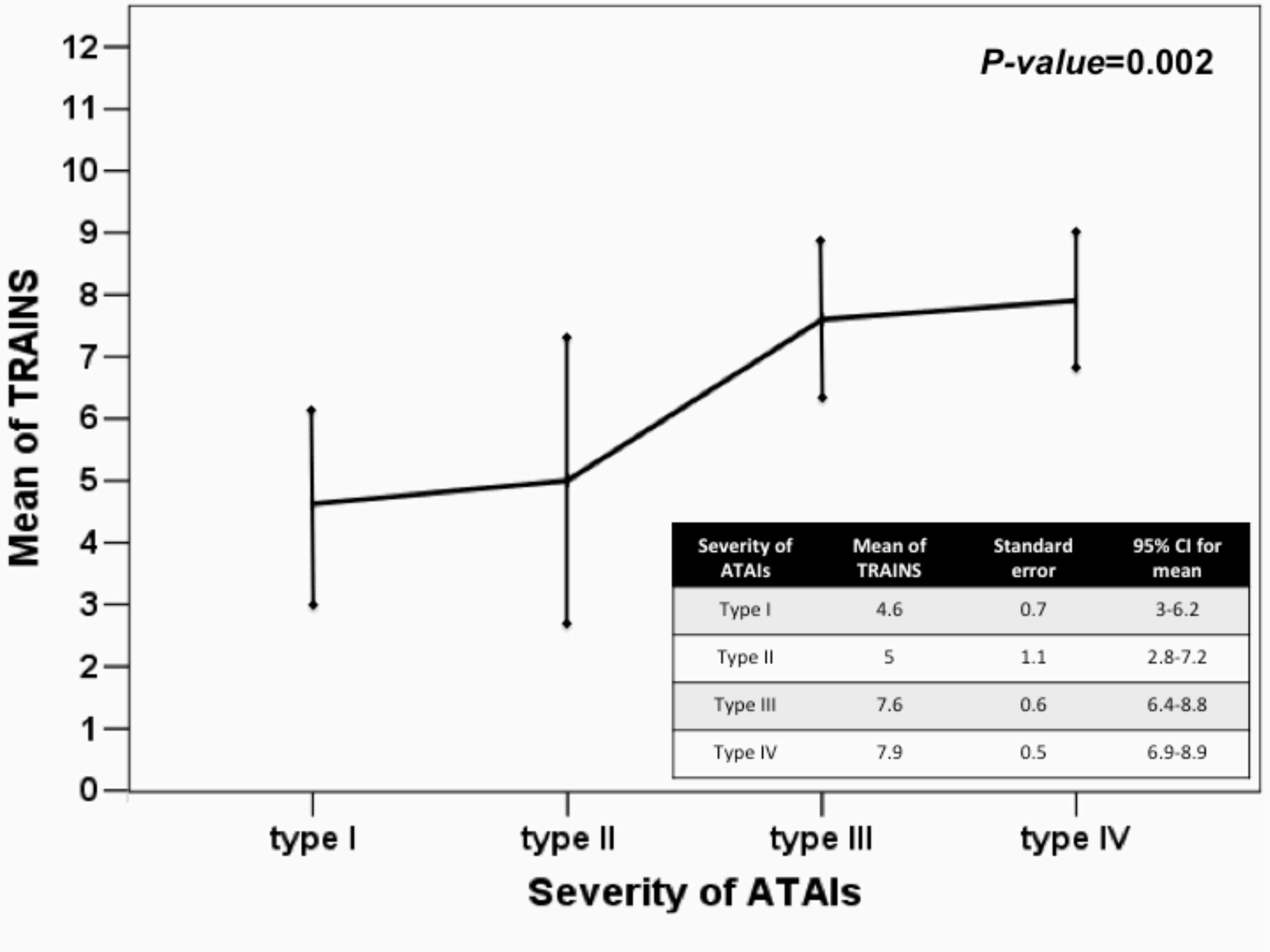


Figure 42. Distribution of patients from the validation dataset according to their result obtained in the TRAINS scoring method.

The one-way ANOVA also confirmed that there was a significant relationship between the TRAINS score and the severity of the aortic injury (types I to IV) (p=0.002) in the validation dataset, as we may observe in Figure 43.



Severity of ATAIs	Mean of TRAINS	Standard error	95% CI for mean
Type I	4.6	0.7	3-6.2
Type II	5	1.1	2.8-7.2
Type III	7.6	0.6	6.4-8.8
Type IV	7.9	0.5	6.9-8.9

Figure 43. Means of TRAINS results among the different degrees of severity of the aortic injuries in the validation dataset (CI= confidence interval).

Conversely, the one-way ANOVA revealed that there were not statistically significant differences between the severity of the trauma defined by any of the classical trauma scores, TRISS (*P*=0.35), ISS (*P*=0.34) or RTS (*P*=0.28), and the severity of the aortic injuries (types I to IV) sustained by trauma patients in the validation dataset (Figure 44).

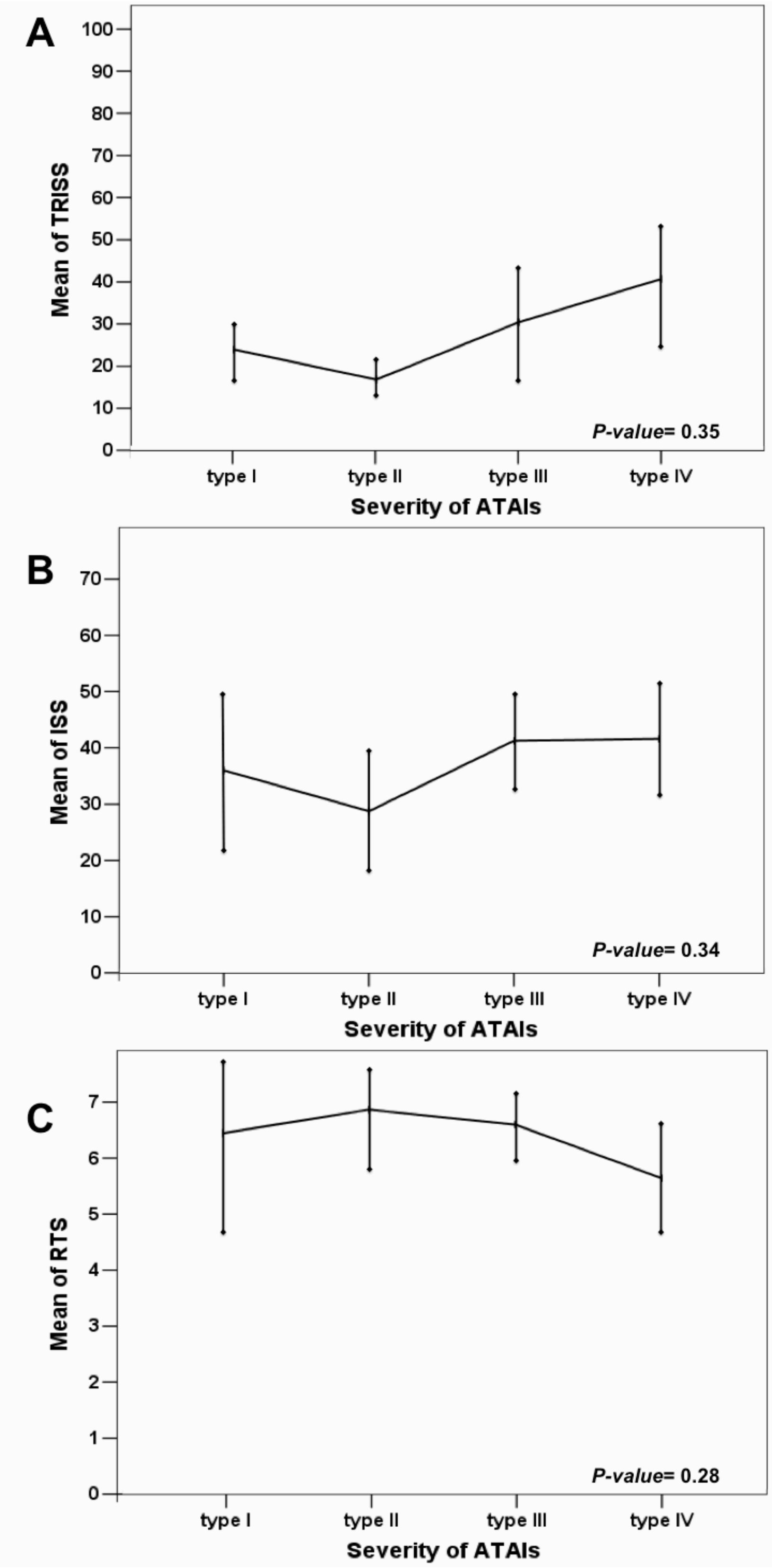


Figure 44. Means of trauma scores, TRISS (A), ISS (B) and RTS (C), among the different degrees of severity of the aortic injuries in the validation dataset (CI= confidence interval).

6. DISCUSSION

6.1. Discussion: importance of ATAI among major trauma patients in Galicia

To date, there is little information regarding the incidence and in-hospital outcomes of ATAIs among major trauma patients in our region. In fact, the precise influence of an associated aortic wall injury on the prognosis of a major trauma patient in our region remained obscure.

In the present study we found that, between 2006 and 2010, the overall importance of ATAIs among major trauma patients with blunt chest trauma in terms of percentage in our institution and in the region of Galicia was 4.4% and 2.5%, respectively. Besides this, the yearly importance of ATAIs in Galicia in terms of percentage was 1.1%-3.3%, whereas it ranged from 2.5%-7.8% in our institution. These findings are consistent with the results of studies in the literature to date. Nevertheless, it must be noted that this study presents a clinical series and that the proportion of ATAIs among major trauma patients is thus underestimated as the analysis did not include those who died due to this catastrophic injuries at the site of accident or the victims who died during transportation. Death at the scene or during transportation is significantly more frequent in patients with an ATAI compared to major trauma patients without aortic injury [21, 22]. According to the results of several other reports, only 10% to 20% of patients with blunt chest trauma and an ATAI reach the hospital alive [2, 21, 22, 315]. Applying the most pessimistic estimate (of only 10% of ATAIs reaching hospital alive) to the Galician population results in approximately 440 cases of blunt ATAI in Galicia during the period 2006-2010. On the contrary, if we consider the less ominous prognosis (20% of ATAIs admitted to hospital alive), this results in around 220 cases of blunt ATAI in

Galicia during the same period. The resulting incidence of this injury in Galicia would be 3 to 6.1 cases per 100,000 inhabitants per year, which is slightly higher than the number reported by other authors such as Feczko et al. [23], Dosios et al. [21] and Teixeira et al. [22].

The graphs (Figures 31 and 32) presented in the *Results* chapter show that, during the period 2006-2010, there was a slight but continual decrease in the total number of major trauma patients admitted to Galician public hospitals per year. This decreasing trend reflects the implementation of vehicle safety and restraint systems (seat belts and airbags), traffic laws enforcement and enhancement of the road environment, but also the enforcement of workplace safety laws and working environment regulations. Nonetheless, the yearly proportion of ATAIs among major trauma patients remained unchanged. Despite the decrease mainly experienced in the total number of road accidents, we can surmise that the lack of decrease, and especially the slight rise, in the proportion of ATAIs among major blunt trauma patients admitted to hospitals is due to the improved survival of ATAI patients who reach the hospital alive as a result of the remarkable advances in trauma care and pre-hospital resuscitation in the last decade.

It is worth to highlight that major trauma patients suffering an ATAI present a different clinical profile than those major trauma patients without associated aortic injury, as we have mentioned in the *section 5.1* of *Results* chapter. The differences in epidemiological profiles of major trauma patients with and without associated ATAI, as demonstrated by the current analysis, refer to the mechanism of accident, the initial clinical presentation, the number and distribution of associated injuries and the prognosis.

Although we have not identified differences in sex distribution between major trauma with or without aortic injury, we have actually reported a significant difference in mean age between both subsets of major trauma patients. Indeed, up to 54.6% of overall ATAIs occurred in major trauma patients between 16 to 35 years old, whereas the age distribution was fairly more homogeneous through the whole age span among major trauma patients without aortic wall injury.

Among the 1,760 major trauma patients admitted to Galician public hospitals between 2006-2010, the cause of accident significantly differed between the subset of patients with ATAI and those without aortic injury. In fact, as we have previously published [256], despite the MVC remains as the main cause of accident among ATAI victims in our series, we have found a higher proportion of MCC, falls and crush traumas and a lower proportion of AVP among patients with ATAI compared to those reported in ATAI victims by other authors in the literature. In both clinical [25, 32, 76] and autopsy [21-24] series, MVC has been identified as the most common mechanism of injury, followed by AVP, MCC, and falls. Furthermore, crush trauma with resulting ATAI is extremely rare in other published series. In Table 23, we compare our results regarding the cause of accident with those reported by other authors.

Author	Year	MVC (%)	AVP (%)	MCC (%)	Falls (%)	Crush (%)	Others (%)
Parmley et al. [2] **(n= 273 pts)**	1958	57.1%	5.8%	1.5%	8.8%	1.8%	9.1%
Eddy et al. [76] **(n=108 pts)**	1990	71.1%	7.7%	17.3%	3.8%	0	0
Feczko et al. [23] **(n=142 pts)**	1992	72%	12%	8%	5%	2%	3%

Fabian et al. [25] **(n=274 pts)**	1997	81%	6.9%	6.9%	2.6%	0	2.6%
Burkhart et al. [24] **(n=242 pts)**	2001	68%	40%	19%	10%	0	2%
Cook et al. [32] **(n=53 pts)**	2006	60.4%	17%	13.2%	7.5%	0	1.9%
Teixeira et al. [22] **(n=102 pts)**	2011	52%	37.3%	6.9%	2.9%	0	1%
Mosquera et al. **(Current series** **n=44 pts)**	**2011**	***40.9%***	***6.8%***	***29.5%***	***11.4%***	***11.4%***	***0***

Table 23. Comparison of our results with those previously published in the literature regarding the distribution of causes of accident among major trauma with ATAI.

We have not only identified significant differences in the mechanism of injury between our series and current literature but also in the anatomic features of the aortic wall injury regarding its location and severity. Among the 44 major trauma patients with ATAI admitted to Galician public hospitals between 2006-2010, the anatomic location of the aortic injuries differed to the reported in most of the clinical series published in the literature hitherto [25, 32, 76]. In fact, we have identified a 43.2% of “atypical or non-isthmal” aortic injuries, which is significantly higher than the 7% to 15% reported in other clinical series [25, 32, 76], which also presented a proportion of injuries at the aortic arch below 6% [25, 32, 76]. Moreover, when comparing the distribution of the site of aortic injury in our series with the anatomic location reported in the autopsy series [21-24] reflected in Table 5 in *section 2.4.3* of *State of the art* chapter, we found a remarkably higher proportion of aortic injuries at the aortic arch (25%) than the 2% to 11% published in the aforementioned autopsy series. It is also worth to mention that this higher proportion of "atypical or non-isthmal" aortic injuries is related to the higher proportion of non-deceleration mechanism of trauma (i.e. crush injuries) found in our series. We have previously published [256] that non-deceleration or non-high speed traumas usually present non-isthmal aortic wall injuries, especially at the level of the aortic arch and the distal descending and abdominal aorta. Actually, aortic injuries in crush thoracic trauma patients seemed to present in a different clinical scenario from aortic injuries in high-speed or deceleration thoracic trauma thus requiring distinct considerations [256]. In the aforementioned study, we found that aortic injuries in crush trauma had associated an increased risk of rhabdomiolysis (mean peak CPK levels in crush trauma ATAIs 7598±3690 IU/L vs. 3645±2506 IU/L in high-speed trauma ATAIs; P=0.041) and subsequent acute renal injury (100% vs. 36.2%; P=0.018), as well as a tendency to develop lower-risk aortic wall injuries (100% in crush patients vs. 43.5% in non-crush patients, P=0.04) [256]. The in-hospital a long-term outcomes of patients suffering an ATAI as a result of a crush trauma turned to be remarkably more benign that in high-speed trauma.

The 72.7% of the 44 major trauma patients with ATAI admitted to Galician public hospitals between 2006-2010 presented a high-risk aortic wall injury (dissection/transection, pseudoaneurysm or frank rupture; types III-IV), whilst the 27.3% developed a low-risk injury (intimal tear <10 mm or hematoma; types I-II). In both multicenter prospective studies of the *American Association for the Surgery of Trauma*, AAST$_1$ [25] and AAST$_2$ [16], the proportion of low-risk ATAIs was 11.4% and 20.2%, respectively. Other clinical recent series have also reported an incidence of low-risk ATAIs from 10% to 14% [32, 33, 116]. Therefore, our series presents a not negligible proportion of low-risk aortic wall injuries, which is higher that the reported by previous authors. We may explain this finding again by the higher frequency of non-deceleration and crush traumas in our series and by the widespread use of MDCT in major trauma patients in Galicia institutions since 2006-2007, which has proven a much higher accuracy in diagnosing minimal aortic injuries [10, 11, 255]. The clinical significance of those injuries still remains obscure and will require further imaging surveillance, as we will comment in advance in *section 6.2* of *Discussion*.

According to our results, major trauma patients sustaining an ATAI present a more ominous prognosis than those without aortic injury, as reflected by a significant difference in in-hospital mortality (38.6% vs. 9.5%; $P<0.001$). Furthermore, regarding major trauma with ATAIs, in-hospital mortality tended to be different among the distinct anatomic locations of the aortic injuries. Indeed, "atypical or non-isthmal" locations as the ascending aorta and the aortic arch presented a significantly higher in-hospital mortality and a worse prognosis.

Furthermore, in the second part of the current research, the development of the TRAINS score commented in *section 6.2* of *Discussion*, we reassured that major trauma patients with associated ATAI had a much higher expected mortality on admission as calculated by TRISS scores in both the score dataset (38.06±36.44% vs. 18.54±24.91%; $P<0.001$) and in the validation dataset (31.46±34.63% vs. 21.39±29.21%; $P=0.055$). In fact, patients with ATAI from both dataset presented more frequently haemodynamic instability and critical status on admission as reflected by a significantly higher proportion of hypotension, need of ETI at site of accident or during transportation and GCS <9. Altogether explains the significantly higher in-hospital mortality found in major trauma patients with aortic injury. In addition, in the current study, trauma patients with ATAI had a much higher proportion of severe abdominal injuries (AIS>3) and severe head injuries (AIS>3). Initial hypotension, severe abdominal injuries and severe head injuries were found to be independent predictors of death in trauma patients with ATAIs by other authors in recent literature [26].

The most frequent cause of death among the patients with an ATAI was aortic-related, either hypovolemic shock or cardiac tamponade, secondary to aortic rupture, or the less common presentation of multisystem organ failure secondary to a malperfusion syndrome. This finding is in accordance with the results of a previous study published by us [36], in which we found that up to the 37.9% of the major trauma patients with non-operatively managed ATAIs developed an aortic-related complication that required surgery or caused the patient's death. In that study we identified two peaks in the rate of complications of conservatively managed ATAIs during the first week and between the first and third months after blunt thoracic trauma [36]. Mantel-Cox regression confirmed that the initial type of aortic lesion (HR: 2.94, P=0.002) and a TRISS score >50% on admission (HR: 1.49, P=0.042) were risk factors for the appearance of potentially lethal aortic-related complications in major trauma patients with ATAIs [36]. The results of that study showed that the natural history of patients with ATAIs presents a marked trend towards developing late aortic-related complications, which stresses the importance of a prompt diagnosis and specific management [36].

In Galicia, the "atypical" characteristics of the major trauma patients with associated ATAI in terms of mechanism of accident, location and severity of the aortic injuries probably obey to demographic characteristics of Galician population, occurring a high proportion of the accidents in rural areas due to certain occupational activities such as cattle-related activities, forestry and tractor and forklift truck accidents.

6.2. Discussion: TRAINS predictive scoring method

This research presents for the first time in the literature a predictive scoring method for ATAIs in major blunt chest trauma patients, which was externally validated in a multicentre study, based on simple variables easy to obtain in the emergency room and proven remarkable both sensitivity and specificity.

The score and the associated algorithm have been designed to rapidly identify major trauma patients at high risk of suffering an ATAI and to provide a framework to optimize resources use and to initiate a prompt medical management to prevent potentially lethal aortic-related complications.

Acute traumatic aortic injury, which is among the most lethal cardiovascular catastrophes, is rarely suspected in major trauma patients upon initial evaluation. Nowadays, the management of ATAIs has evolved thanks to the advent of MDCT and other advances in imaging technology [60], clinical management with aggressive control of both blood pressure and cardiac contractility for patients who reach the hospital alive [12], the shift toward the use of aortic endovascular repair techniques [15], and the institution of delayed surgical treatment after other associated critical injuries have been stabilized [16]. Nevertheless, an important number of patients may not completely benefit of all the advances achieved in the ATAI management because of a delay in the diagnosis of aortic injury, which may lead to catastrophic aortic-related complications [36]. Furthermore, the imaging diagnosis of some ATAI requires a specific arterial MDCT with MPR or an IVUS study [10, 11]. On the other hand, if every major trauma patient undergoes an arterial MDCT with MPR for a potential ATAI, the cost and level of radiation exposure would be prohibitive. Indeed, nowadays some concerns [123, 124] have been raised about excess diagnostic radiation exposure during high-resolution imaging diagnosis as we have previously commented in the *chapter 2.6.2.3 of the State of the art in ATAIs*. Recent studies have proven that a typical patient with traumatic injuries who undergoes irradiation at a young age incurs an increased cumulative lifetime risk of developing cancer [123].

In daily practice, on admission CXR is used to provide data to guide suspicion of ATAIs in major trauma patients. A widened mediastinum [100] and variations such as a left mediastinal width ≥6 cm or more and a mediastinal width ratio ≥0.60 [94], as well as other CXR findings (rightward tracheal, esophageal, and/or nasogastric tube deviation; left mainstem bronchus depression; and a left apical cap [96, 97, 99]) are frequently associated with the diagnosis of an ATAI and are used in the decision to proceed to more advanced imaging tests. Nonetheless, although combining the most sensitive radiographic signs may improve sensitivity up to 90% in certain series, there is a simultaneous decrease in specificity (even <50%) which fails to provide a sufficient negative predictive value to avoid the performance of unnecessary imaging tests [60, 100]. In addition, it has been reported in the literature that up to 30% of patients with ATAIs may not present mediastinal abnormalities [97, 316]. On the contrary, patients with mediastinal haemorrhage have no more than a 20% probability of major thoracic vascular injury [113]. The vast majority of major trauma patients (97.9% of the patients in our study) had a CXR taken in the supine position using portable imaging equipment. Thus, in a significant number of cases, the interpretation of CXR findings in major trauma patients may be difficult due to the poorer technical quality of supine radiographs taken using portable equipment, including aspects such as patient's rotation, degree of inspiration, and adequacy of radiographic penetration, and each of these technical shortcomings can produce invalid signs of ATAIs [92, 100]. In fact, in our study the accuracy on admission CXR of a widened mediastinum (greater than 8 cm and/or 25% of the width of the thorax), tested as a single predictive sign, was limited with a sensitivity of 78.9% and a specificity of 75.9% in the score dataset. It was clear that in order to improve on the relatively low accuracy of CXR for the detection of ATAIs, a more specific screening test was necessary. In our analysis, the beta-coefficient of a widened mediastinum provided by the binary stepwise forward logistic regression was 3.42 (Table 17). That result involved that, after rounding its beta-coefficient to the closest integer value, a widened mediastinum would have received an assigned score of 3 points. Such score would entail i.e. to completely ignore a large mediastinum on a hypothetic trauma patient with a score < 4, a practice which is clearly against the current standard of care and of almost impossible implementation. That is the reason why a widened mediastinum was forced to entail a positive test by itself (it is, score ≥4), being rounded to 4 rather than 3 points. Furthermore, all the patients with ATAI and widened mediastinum in the score dataset presented another associated risk factor apart from the widened mediastinum, which altogether would have anyway entailed a positive test (true positives): 95% of lung contusion; 73.3% of hemothorax; 76.7% of hypotension; 21.6% long bone fracture; 51.7% of pelvic fracture and 25% of left scapula fracture. It means that, even assigning 3 points to a widened mediastinum, all the patients with ATAI and a widened mediastinum would have equally scored 4 or more points in the TRAINS score; thus, obtaining anyway a positive test and remaining as true positives. On the contrary, all major trauma patients without an ATAI and with widened mediastinum presented another associated predictive factor, resulting again in positive tests (false positives). This subgroup of patients, NATAI with widened mediastinum, presented a 94.5% of lung contusion; 75.3% of hemothorax; 54.8% of hypotension; 23.3% of pelvic fracture; 8.2% of left scapula fracture and 1.4% long bone fracture. We may surmise then that the rounding performed to the variable widened mediastinum would not have somehow jeopardized the accuracy and internal validity of the test.

Even considering such modification, we developed a highly predictive but easy scoring method based on clinical and CXR data with a sensitivity of 93.4% (87.2%-99.6%) and a specificity of 85.9% (81.8%-89.9%) in our centre population (score dataset) and with a sensitivity of 92.3% (86.1%-100%) and a specificity of 85.1% (80%-90.2%) after an independent external multicentre validation process (validation dataset).

When developing a predictive score for an uncommon but potentially lethal condition such as the traumatic aortic injury, it is vital to strike a balance between a high sensitivity and an acceptable specificity, which in our study was achieved by using a cut-off value of ≥4 points. Moreover, a small number of false negatives were obtained using this cut-off value of ≥4 points, with five patients (1.8%) in the score dataset and four patients (2.2%) in the validation dataset, where all of them had small intimal tears or intramural hematomas (types I-II injuries). Furthermore, even if we analyse only the accuracy of TRAINS score among low degree aortic injuries (types I-II), the sensitivity and the specificity of the score remain as high as 86.1% and 85.9%, respectively.

As other authors have found [116], the conventional trauma risk scores (ISS, RTS and TRISS) failed to show statistical relationship between the severity of the trauma and the degree of severity of the aortic injury (types I to IV) in both datasets. Thus, the conventional trauma severity scores are useless to raise diagnostic suspicion of ATAI. On the contrary, the TRAINS score has proven to be related with the severity of the aortic injury in both datasets. In fact, the greater the TRAINS score, the more severe the aortic injury.

In order to enable a prompt identification of major trauma patients at risk of suffering a potentially lethal aortic injury, we currently recommend that all patients with a TRAINS score ≥4 undergo an optimal medical control of cardiac contractility, blood pressure and heart rate, and advocate a specific aortic MDCT protocol combined with a TEE; the latter especially in unstable and/or intubated patients. Medical therapy should include intravenous infusion of a vasodilator to avoid hypertension and limited intravenous fluid infusion once the systolic blood pressure exceeds 100 mmHg. Beta-blockers are the drugs of choice for initial medical stabilization because they control both the heart rate and blood pressure [14]. The systolic blood pressure should be titrated to approximately 100 mmHg, and the heart rate to <60 bpm [12-14]. This practice may only deviate in the respect that patients with evidence of increased intracranial pressure must be considered immediate operative candidates if other factors permit in order to prevent secondary brain injury associated with the decrease in cerebral perfusion pressure that accompanies hypotensive medical therapy [32]. Likewise, patients with a score ≥4 (high risk of ATAI) should undergo a three-phase vascular MDCT from the thoracic inlet to the symphysis pubis including an unenhanced phase, an arterial contrast-enhanced phase, and a venous or portal phase. Whenever the score is ≥4 it is mandatory to generate oblique reconstructions that resemble the images obtained in conventional angiography, as well as sagittal, coronal and MPR [107]. In contrast, patients with a score <4 (low-risk of ATAI) should be managed with simple CXRs, data from extended focused assessment with sonography for trauma (eFAST) and, when indicated due to a suspected non-aortic injury (i.e. a non-vascular thoracic injury or an intraabdominal solid organ injury), a less aggressive thoracic or thoraco-abdominopelvic protocol of two-phase MDCT. The latter minimizes the contrast and radiation exposure of the patient compared to a three-phase vascular MDCT. Using a standard trauma (non specific arterial) MDCT scan protocol without MPR, some high degree ATAI can be diagnosed, but up to 10-20% of less severe aortic injuries [116] can be missed. Although low degree aortic injuries usually do not pose a life-threatening risk at the moment of trauma admission, its long-term natural history is not well-known. Those less severe aortic injuries may spontaneously resolve, remain stable on imaging controls or, on the contrary, lead to potential adverse consequences as formation, enlargement and rupture of pseudoaneurysm; embolism of loose intima, or thrombus; or progressive dissection of the aortic wall [33, 36, 81, 116, 220, 252, 255, 317].

Other alternative cut-off values such as a score of ≥5 points were rejected because, despite providing a higher specificity (94.7%), the decrease in sensitivity (74.7%) would probably mean that the diagnosis of a significant number of traumatic aortic injuries would be missed, which is not affordable from a clinical point of view. Conversely, a cut-off value of ≥3 points with a higher sensitivity (97.2%) presented an unacceptably low specificity (53%), which would involve the overuse of advanced thoracic imaging tests (TEE, MDCT) in a large number of patients without aortic injury (false positives). Thus, a score with a low specificity might entail an unnecessary increase in hospital resources (e.g., intensive care unit surveillance) and financial costs and, moreover, unnecessary and deleterious exposure to nephrotoxic contrast agents and radiation.

We have proposed an algorithm for the management of any patient with major blunt chest trauma and a high risk of ATAIs combining TRAINS with the international recommendations for advanced imaging tests [10, 11] and medical therapy [12-14] (Figure 45).

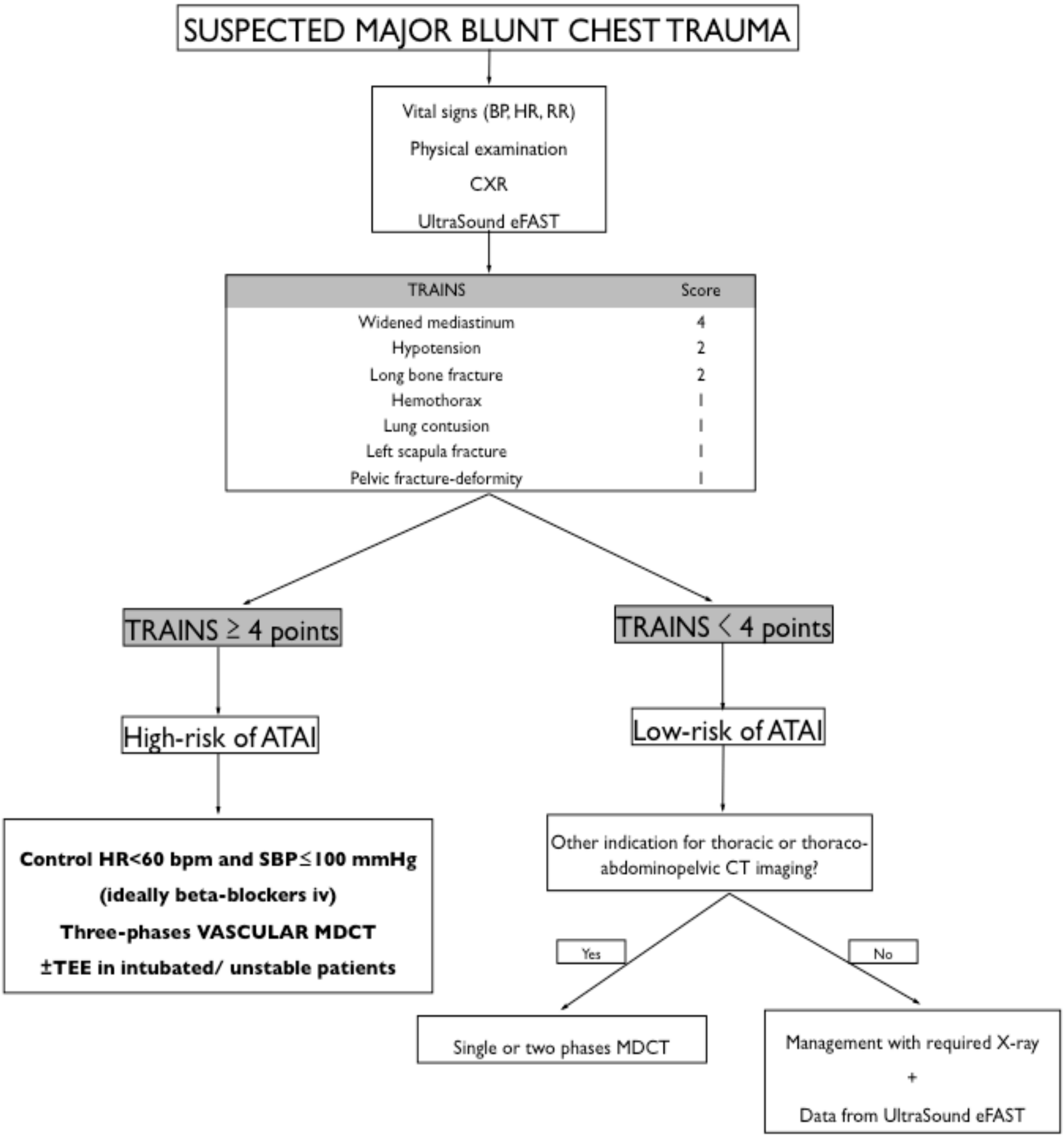


Figure 45. Algorithm for management of major trauma patients with ATAI. This proposed algorithm for the management of any patient with major blunt chest trauma and with a high risk of ATAIs has been designed according to the international recommendations for advanced imaging tests [10, 11] and medical therapy [12-14]. (BP= blood pressure; HR= heart rhythm; RR: respiratory rate; CXR= chest X-ray; eFAST= extended focused assessment with sonography for trauma; MDCT= multidetector computed tomography).

Although other authors examined clinical factors that might be associated with aortic injury, our research is different from previous works for several reasons. First, we used a study design with four NATAI control patients per ATAI patient, thereby greatly increasing the statistical power of the study for the relatively uncommon ATAI. Second, in addition to measuring the clinical predictors separately, we used binary logistic regression to determine whether or not each factor was a predictor, even accounting for the effects of all of the other predictors. Third, and of the utmost importance, we developed a methodologically rigorous yet easy, fast and simple predictive scoring system for traumatic aortic injury, which, to the best of our knowledge, is the first one to be independently validated in a multicentre study. It is worth emphasizing that the process of external validation is of paramount importance for checking the validity of a predictive model across other geographic areas [318].

Apart from the previously mentioned CXR findings suggestive of ATAI described by other authors [94, 96, 97, 99, 100], clinically relevant correlations have been reported between non-mediastinal injuries and ATAIs in both clinical and autopsy series. Fabian et al. [25] pointed out the fact that 93 (33.9%) of the 274 patients with ATAIs who were enrolled in a multicentre trial sponsored by the *American Association for the Surgery of Trauma* (AAST_1) presented pelvic or long bone fractures. More recently, in a clinical series, Cook et al. [32] described the incidence of associated injuries among 53 patients with an ATAI: 22.6% of myocardial contusions, 49.6% of pulmonary injuries, 45.3% pelvic injuries and 50.9% of long bone fractures.

After reviewing 275 cases of blunt ATAIs, Parmley et al. [2] found that 38% of these patients had an associated cardiac injury. This classic study also found that 80% of the patients with combined aortic and cardiac injuries and more than one half of the patients with an aortic injury had sustained additional injuries that were severe enough to cause their deaths [2].

In an autopsy series of 242 fatal ATAI victims reported by Burkhart et al. [24], associated lung injuries and lower extremity fractures were present in 53% and 43% of the cases, respectively. Likewise, in a more recent series of 304 autopsies from blunt trauma in which 102 (34%) ATAIs were identified, Teixeira et al. [22] found that patients with ATAIs were significantly more likely to have other associated injuries: cardiac injury (44% vs. 25%, $P = 0.001$), hemothorax (86% vs. 56%, $P < 0.001$), pelvic fracture (40% vs. 26%, $P = 0.014$), rib fractures (86% vs. 72%, $P = 0.006$) and intra-abdominal injury (74% vs. 49%, $P < 0.001$) compared with patients without ATAI.

In our study, patients with ATAIs were significantly more likely to have a wide range of associated injuries when compared to major trauma patients who did not sustain aortic injuries. In fact, many of the coexisting injuries of blunt major chest trauma patients in both the ATAI and NATAI groups were comprised of extrathoracic trauma. At least one severe (AIS>3) extrathoracic injury was recorded in all the trauma patients included in our study. Therefore, our experience is consistent with the results of studies in the literature in many respects, whilst also providing some new insights into combining radiological and clinical findings to improve the diagnosis and management of ATAIs.

Blackmore et al. [87] published a traumatic aortic injury prediction rule based on a single-centre retrospective case-control study. Although innovative, this study presented several shortcomings; for example, the number of cases was very low, with only 31 patients with an ATAI. Because none of the simple predictors reached statistical signification in the logistic regression analysis, the authors had to resort to composite predictors, which jeopardized the utility of the prediction rule in an Emergency or Trauma Department. Besides this, the study lacked an external validation in other populations to ensure generalizability.

In fact, a more recent re-evaluation of those clinical predictors by Kirkham et al. [88] showed that only four factors (abdominopelvic injury, thoracic injury, hypotension, and being unrestrained) were actually predictive. Furthermore, the combination of three or four factors only resulted in a 2% chance of an ATAI [88].

One factor with our model that differs from previous ones is that all types of mechanisms of blunt major trauma were analysed and their potential influence as risk factors for traumatic aortic injury was assessed. Although we found that the variable MVC was statistically significant on bivariate analysis, the logistic regression analysis did not confirm it as a potential risk factor for traumatic aortic injury.

The CXR obtained during the initial assessment at the trauma bay, in combination with the clinical examination, remains the gold standard for the diagnosis of suspected traumatic aortic injuries.

To the best of our knowledge, this is the first predictive scoring method of ATAIs in major trauma patients to be externally validated in a multicentre study. Apart from both an internal and external multicentre validation, the strength of our research lays in the fact that comprehensive data points were analysed in order to answer a clinically relevant question. The variables included in the final score are easily determined upon clinical examination and CXR and are therefore ready while the patient is still in the trauma bay. This method also overcomes a weakness present in other models that use variables such as AIS scores from each body region, which are dependent on the performance of advanced image tests [127].

On the other hand, the TRAINS algorithm may enable optimization of the use of clinical and diagnostic resources to provide an early and accurate diagnosis of patients at a high risk of ATAI, reducing admission costs and the exposure to nephrotoxic contrast agents and radiation in low-risk patients. Besides, TRAINS score is able to raise suspicion of ATAI even in trauma cases with low-degree aortic injuries, thus recommending the performance of a specific arterial MDCT with MPR and avoiding the misdiagnosis of aortic injuries.

6.3. Limitations

There are limitations with our model that need to be considered, including the limitations inherent in any retrospective study. The model only includes the variables available in our dataset; there may be other more complex variables that could potentially influence the diagnosis but which are not routinely collected. Consequently, as the purpose of this model is to guide clinicians prior to the development of definitive diagnosis techniques, such factors would be impossible to predict. Finally, the score dataset was obtained from a long time period during which substantial diagnostic and therapeutic advances were incorporated. Hence, we must admit a potential non-contemporaneous control (major trauma patients without ATAI) bias because control patients were obtained from the period 2009-2010. Nevertheless, we consider that using a more recent control group decreases the chance of missclasification (i.e. including as controls patients with aortic lesions), a positive value for the control group.

The rounding of the variable widened mediastinum to 4 points might jeopardize the score from a pure statistical point of view, but this modification improves the applicability of the score in the everyday clinical practice. All the patients with ATAI and widened mediastinum in the score dataset presented another associated risk factor. It means that, even assigning 3 points to a widened mediastinum, all the patients with ATAI and a widened mediastinum would have equally scored 4 or more points in the

TRAINS score; thus, obtaining anyway a positive test (true positives). On the contrary, all NATAI patients with widened mediastinum presented another associated predictive factor, resulting anyway in positive tests (false positives). Therefore, the rounding performed in a widened mediastinum would not have somehow jeopardized the accuracy and internal validity of the test. Moreover, in spite of the aforementioned modification, the score maintained a great accuracy in the external validation process performed in a current trauma population from three different geographic areas.

The simplicity of the scoring method, the fact that it does not depend on the result of complex diagnostic tests and its validation in a contemporaneous multicentre population overcomes these shortcomings.

7. CONCLUSIONS

In relation with the 2 main objectives outlined at the beginning of this research, we may summarise our conclusions as follows:

I. Objective I- Epidemiology of ATAI in Galicia

a) The overall importance in terms of percentage of ATAIs among major trauma patients with blunt chest trauma between 2006 and 2010 in our institution (CHUAC) and region (Galicia) was 4.4% and 2.5%, respectively. Likewise, the yearly proportion of ATAIs among major trauma patients in Galicia was 1.1%-3.3%, whereas it ranged from 2.5% to 7.8% in our institution. After estimation of the number of major trauma patients with ATAI who die at the site of accident or during transportation, the actual resulting incidence of ATAI in Galicia would be 3 to 6.1 cases per 100,000 inhabitants per year. A more comprehensive study in the future combining data from clinical and autopsy series is required to truly determine the importance in percentage terms of ATAI among major trauma patients.

b) The yearly proportion of ATAIs among major trauma patients has been slightly increasing, probably due to the advances in trauma care and pre-hospital resuscitation that have reduced the number of ATAI victims who die at the scene or during transportation. This finding stresses the need for a future study enrolling cases from both clinical and autopsy series.

c) Our research has confirmed that in Galicia major trauma patients with associated ATAIs present a different epidemiological profile, prognosis, initial clinical presentation and number and distribution of associated injuries.

d) In Galicia, while major trauma patients without aortic injury distribute fairly homogeneously through the whole age span, ATAIs concentrate among 16 to 35 years old trauma patients, where 54.6% of overall ATAI occurs.

e) The cause of accident significantly differs between the subset of trauma patients with ATAI and those without aortic injury. The MVC is the commonest cause of accident among ATAI victims in Galicia, but we have found a higher proportion of MCC, falls and crush traumas and a lower proportion of AVP among patients with ATAI compared to those reported in ATAI victims by other authors.

f) The proportion of "atypical or non-isthmal" aortic injuries (43.2%) is significantly higher than the 7% to 15% reported in other clinical series, also highlighting a remarkably higher proportion of injuries at the aortic arch (25%).

g) Major trauma patients with ATAIs present with haemodynamic instability on admission more frequently than major trauma patients without aortic injury. The former also have a higher proportion of severe extra-thoracic injuries, which justify their worse prognosis.

h) Major trauma patients with associated ATAIs had a higher expected mortality rate on admission than major traumas without ATAI and also presented an actual higher in-hospital mortality rate, which was mostly caused by aortic-related complications, mainly aortic rupture or distal malperfusion syndrome.

i) In-hospital mortality tended to be different among the distinct anatomic locations of the aortic injuries, especially in "atypical or non-isthmal" locations, as the ascending aorta and the aortic arch, which present a significantly higher in-hospital mortality and worse prognosis.

II. Objective II- Predictive score of the risk of ATAI in major trauma patients

a) The accuracy of a widened mediastinum on admission CXR as a predictive sign of ATAI in our study was significantly limited with a sensitivity of 78.9% and a specificity of 75.9%. However, the combination of clinical examination findings and CXR on admission has been shown to accurately diagnose suspected traumatic aortic injuries.

b) We developed a contemporaneous multivariate prediction model for traumatic aortic injury after major trauma with a sensitivity >93% and a specificity >85%. The small number of ATAI patients who were misdiagnosed by TRAINS (false negatives) presented low-degree aortic injuries in all cases.

c) The scoring method proved its accuracy in both an internal and an external validation process. TRAINS demonstrated its ability to diagnose ATAIs among major trauma patients with a sensitivity >92% and a specificity >85% in a current multicentre population of major trauma patients, thus confirming its applicability at the current time and in different geographical areas.

d) We have demonstrated that the conventional trauma risk scores (ISS, RTS and TRISS) fail to show statistical relationship between the severity of the trauma and the degree of severity of the aortic injury (types I to IV). Thus, the conventional trauma severity scores are useless to cast suspicion on the diagnosis of ATAI. On the contrary, TRAINS score has proven to be related with the severity of the aortic injury and to be useful even in the diagnosis of low-degree ATAIs.

e) The TRAINS score and associated algorithm have been designed to be used in daily practice to easily and rapidly identify major trauma patients who are at risk of aortic injury, thus avoiding unnecessary costs and radiation exposure in low-risk trauma patients. On the other hand, the TRAINS score may raise suspicion of ATAI even in the cases of low-degree aortic injuries, which require a close imaging surveillance to determine whether those patients will need a further intervention.

f) The TRAINS algorithm is also useful for resource allocation planning, enabling clinicians to refer patients at high risk of traumatic aortic injuries to specialized units, providing the ability to rapidly diagnose and therapeutically manage this critical subset of trauma patients in order to avoid potentially lethal aortic-related complications.

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9. APENDICES

9.1.APPENDIX I: Publications

- Mosquera VX, Herrera JM, Marini M, Estevez F, Cao I, Gulías D, Valle JV, Cuenca JJ. Mid-term results of thoracic endovascular aortic repair in surgical high-risk patients. *Interact Cardiovasc Thorac Surg* 2009;9(1):61-5.
- Mosquera VX, Marini M, Lopez-Perez JM, Muñiz-Garcia J, Herrera JM, Cao I, Cuenca JJ. Role of conservative management in traumatic aortic injury: comparison of long-term results of conservative, surgical, and endovascular treatment. *J Thorac Cardiovasc Surg* 2011;142(3):614-21.
- Mosquera VX, Marini M, Muñiz J, Lopez-Perez JM, Gulías D, Cuenca JJ. Aortic injuries in crush trauma patients: Different mechanism, different management. *Injury*. 2011 Oct 11. [Epub ahead of print] DOI: 10.1016/j.injury.2011.09.022
- Mosquera VX, Marini M, Cao I, Gulias D, Muñiz J, Herrera-Noreña JM, Cuenca JJ. Traumatic aortic injuries associated with major visceral vascular injuries in major blunt trauma patients. *World J Surg. 2012 Jul;36(7):1571-80.*
- Mosquera VX, Marini M, Gulias D, Cao I, Muñiz J, Herrera-Noreña JM, Lopez-Perez JM, Cuenca JJ. Minimal traumatic aortic injuries: meaning and natural history. *Interact Cardiovasc Thorac Surg. 2012 Jun;14(6):773-8. Epub 2012 Mar 21.*
- Victor X Mosquera, Milagros Marini, Javier Muñiz, Vanesa Asorey-Veiga, Belen Adrio-Nazar, Ricardo Boix, José M Lopez-Perez, Gonzalo Pradas-Montilla, José J Cuenca. Traumatic Aortic Injury Score (TRAINS): an easy and

simple score for early detection of traumatic aortic injuries in major trauma patients. *Intensive Care Med. 2012 May 23*. DOI: 10.1007/s00134-012-2596-y.

9.2.APPENDIX II: Unpublished data. Manuscripts under review

- Mosquera VX, Marini M, Muñiz J, Asorey-Veiga V, Adrio-Nazar B, Herrera-Noreña JM, Pradas-Montilla G, Cuenca JJ. Blunt traumatic aortic injuries of the ascending aorta and aortic arch: a clinical multicentre study. *Submitted to*: *Injury. Under Review.* JINJ-D-12-00337