BLUNT TRAUMA ASSOCIATED WITH INCREASED CARDIOVASCULAR MORBIDITY

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Cardiovascular diseases and trauma are two major public health issues. Evidence from numerous clinical case reports suggests that trauma may lead to various cardiovascular disorders, such as acute myocardial infarction, cardiac valve disorders and arrhythmias. Various mechanisms of such associations have been suggested; however, no population based studies have been conducted. Population-based studies are important in that they reduce the potential for selection bias and confounding, both of which may limit the interpretation of case reports. In addition, population based studies which include control groups provide quantitative estimates of association.

We hypothesize that trauma is significantly associated with increased risk for certain cardiovascular disorders. To examine this issue, we conducted a cross-sectional analysis of the association between certain types of trauma (i.e. blunt cardiac injury (BCI), blunt thoracic injury, blunt abdominal/ pelvic trauma) and certain cardiac disorders (cardiac valve insufficiency and acute myocardial infarction) based on a large database of all hospital discharges from 19 states during a one-year period. We also conducted a matched case-control study of the association between blunt cardiac and thoracic injury and cardiac arrhythmias. Both the exposure (trauma) and the disease (cardiovascular disorders) were identified based on ICD-9-CM codes. Various confounding factors have been identified through the database. Unadjusted, multivariate logistic and the conditional adjusted multivariable regression analyses were performed.

Independent of potential confounding factors, discharge for BCI was associated with a 12-fold increased risk for tricuspid valve insufficiency, incompetence, regurgitation or stenosis and a 3.4-fold increased risk for aortic valve insufficiency, incompetence, regurgitation or stenosis. Independent of confounding factors and coronary arteriography status, direct trauma to the heart was associated with a 3-fold increased risk for acute myocardial infarction in persons 46 years or older. When the diagnosis of acute myocardial infarction was confirmed by coronary arteriography, BCI was associated with a 5-fold risk elevation among patients 46 years and older and a 44-fold elevation among patients 45 years and younger. Abdominal or pelvic trauma, irrespective of confounding factors and coronary arteriography status, was associated with a 70% increase in the risk of acute myocardial infarction among patients 45 years and younger and a 3-fold increase among patients 46 years and older. We also found that after adjusting for potential confounders, patients 45 years and younger diagnosed with BCI had 13-fold increase in the risk of cardiac arrhythmia.

This research has public health significance because it represents one of very few attempts to look at the association between two major health issues - namely trauma and cardiovascular disorders at such a large population based level. With the findings that several types of traumatic injury (such as thoracic, cardiac, abdominal and pelvic) are associated with an increased risk of specific cardiovascular disorders – namely – cardiac valve insufficiency, acute myocardial infarction and cardiac arrhythmias, it appears that trauma may play an important and heretofore largely unrecognized role in a portion of the national burden of cardiovascular morbidity and mortality.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.   INTRODUCTION

1.1.   INJURIES

1.1.1.   Overview

An injury is damage to any part of the body resulting from acute exposure to thermal, mechanical, electrical or chemical energy.(MacKenzie, 2000a) There are more than 6 million people who are injured and about 200,000 who die in motor vehicle accidents annually around the world.(Baker et al., 1992) In the US, injury occurs in one in four people during a given year.(MacKenzie, 2000a) Over 400 people die due to injury in this country everyday.(MacKenzie, 2000a) Injury is one of the leading causes of death over several age groups. (MacKenzie, 2000a) Injury from unintentional and intentional causes, for example, is the leading cause of death for children and adults between the ages of 1 and 44 years. (MacKenzie, 2000a) It has been estimated that there are 18 hospital discharges and 250 injury-related visits to hospital emergency department for every injury death. (MacKenzie, 2000a)

1.1.2.   Motor vehicle accidents

In general, among persons 6 to 27 years, motor vehicle crashes are the leading cause of death in the United States. (Anonymous) Such crashes account for approximately 1 million years of potential life lost before age 65 annually.(Anonymous) However, many more people are injured and survive motor vehicle crashes than die: 40,000 persons die because of motor vehicle

accidents while about 5 million persons are injured. (Anonymous) Motor vehicle crashes are the most frequent cause of cardiovascular trauma due to the forces of deceleration that can damage the intrathoracic structures. (Keough and Pudelek, 2001)

1.1.3. Thoracic trauma

In general, blunt thoracic injury represents a significant component of the morbidity and mortality from general trauma. About 20% of hospitalized trauma cases per year in the US have thoracic trauma as a component. (LoCicero and Mattox, 1989) The incidence of hospitalized thoracic trauma in the US is 12 per million population per day or about 100,000 cases per year. (LoCicero and Mattox, 1989) Overall, in the US, thoracic injury is responsible for approximately 16,000 deaths per year. (LoCicero and Mattox, 1989) About 25% of deaths due to injury are attributed to thoracic trauma do not require surgical intervention.(LoCicero and Mattox, 1989)

Thoracic trauma is often associated with cardiac trauma due to anatomical proximity of the heart to the chest wall. In a few autopsy and clinical case studies, the incidence of cardiac injury varied from 10% to 75% in the presence of chest injury. (Leinoff, 1940) In addition to cardiac injuries, thoracic trauma may also lead to injury of lungs, pleura, thoracic great vessels, diaphragm, trachea and oesophagus.(LoCicero and Mattox, 1989; Anonymous, 1991) Both penetrating and blunt forces can cause thoracic trauma. The most common feature of penetrating thoracic trauma is pneumothorax usually caused by gun shot or a wound. (LoCicero and Mattox, 1989; Anonymous1991) Rapid deceleration resulting from falls and direct impact and compression from motor vehicle crashes are common mechanisms of blunt thoracic injury. (LoCicero and Mattox, 1989; Anonymous, 1991) Approximately 25% of hospitalized injuries in motor vehicle accidents involve the chest. (LoCicero and Mattox, 1989; Anonymous1991) On

the other hand, more than 60% of major chest trauma cases are related to motor vehicle crashes. (LoCicero and Mattox, 1989; Anonymous1991) Physicians should be alert about cardiac or vascular trauma even in the case of mild form of thoracic injury since the degree of external trauma may not fully predict the severity of internal injury.

1.1.4. Abdominal trauma

In general, blunt abdominal trauma is thought to be the most common cause of preventable deaths and missed injury. (Demetriades, 2004) There is also evidence that abdominal trauma may cause cardiovascular injury. (Demetriades, 2004) An incidence of blunt abdominal trauma following motor vehicle accidents has been estimated at 14%. (Demetriades, 2004) The incidence of intra-abdominal injuries of 6% was found in victims of falls from heights of more than 15 feet. (Demetriades, 2004) As with thoracic trauma, both penetrating and blunt forces can cause abdominal trauma.

Cases of combined abdominal trauma and cardiac injury have been reported. (Jokl and Greenstein, 1944) (Gayet et al., 1987) The mechanism of such trauma was described by Beck (Beck and Bright, 1933) and was explained by the increase of intravascular hydrostatic pressure which occurs with sudden compression or crushing of the abdomen. (Beck and Bright, 1933; Begoian and Iakushev, 1980; Oleinik et al., 1985; Kellert, 1917; Rea et al., 1969; Dubrow et al., 1989; Parry and Wilkinson, 1997) Sudden elevation of intra-aortic pressure caused by external impact to the abdominal area may result in rupture of the coronary vessel particularly if the aortic valve was closed during the traumatic impact during diastole. In addition to cardiovascular trauma, blunt abdominal injury most frequently results in injury to the spleen (30%), followed by the liver (25%), and the kidney (20%). (Demetriades, 2004) Significant intra-abdomianl injuries

were found to be associated with the presence of a seatbelt sign.(Demetriades, 2004) However, seatbelt use has been reported to have no effect on the incidence of intra-abdominal injury.(Demetriades, 2004)

1.1.5.   Cardiovascular trauma

1.1.5.1.   Overview

Cardiovascular trauma is the second leading cause of death after central nervous system injury.(Mayfield and Hurley, 1984) The true incidence of cardiovascular trauma is unknown because there are no standard diagnostic approaches employed to fully evaluate this condition. In addition, in some patients, cardiovascular trauma could be initially asymptomatic which makes it difficult to diagnose.

Cardiac injuries are usually represented by non-specific ST-T wave changes on ECG. (Harthorne et al., 1967a) The most common form of cardiac trauma is BCI, formerly know as "myocardial contusion". (Turner, 1990) Other forms may include pericardial injury (Mattila et al., 1975; McCabe et al., 1974; Arom et al., 1977; Sbokos et al., 1977; King and Sapsford, 1978; Larrieu et al., 1980), cardiac laceration (Layton et al., 1979; Smith et al., 1976; Hendel and Grant, 1981; Patton et al., 1981; Williams et al., 1981), ventricular aneurysm (Sharratt et al., 1976; Berkoff et al., 1977; Rheuban et al., 1981), ventricular septal defects (Anyanwu, 1976a; Midell et al., 1975; Rubio et al., 1978; Danzl et al., 1980; Pellegrini et al., 1980; Pickard et al., 1980), coronary injury (Harthorne et al., 1967a; Jones, 1970a; Ginzburg et al., 1998a; Fu et al., 1999; Fang and Li, 1994; Atalar et al., 2001a; Heymann and Culling, 1994a; Candell et al., 1979a; Kahn and Buda, 1987a; Foussas et al., 1989a; Heyndrickx et al., 1974a; Haas et al., 1968; Goulah et al., 1988; Kohli et al., 1988a; de Feyter and Roos, 1977a) intracardiac fistulae (Alter et

al., 1977; Hines et al., 1977; Rayner et al., 1977), cardiac valve injury (van Son and Starr, 1995; Cho et al., 1995; van Son et al., 1994; Anyanwu, 1976a; Bailey et al., 1969; Bryant et al., 1973a; Weldon et al., 1972; Wilke et al., 1997; Bortolotti et al., 1997; Chi et al., 1977; Cahill et al., 1972; Cleveland and Cleveland, 1974; Bruschi et al., 2001; Cuadros et al., 1984; Van Roye and Zienkowicz, 1989) and iatrogenic cardiac injury.(Sethi et al., 1977; Abbott et al., 1978; Bodily and Fischer, 1979; Culliford and Spencer, 1979; Venkataraman and Bilitch, 1979; Wong et al., 1979; Silverman et al., 1980)

Cardiovascular trauma can be classified based on the site of the lesion as cardiac or vascular injury. It can be also classified based on the mechanism of injury (i.e. blunt versus penetrating). The major focus of this research is blunt trauma to the heart (or blunt cardiac injury) although it is also important to review blunt vascular injury since this type of trauma is a component of the mechanism of traumatic myocardial infarction.

Blunt vascular injury is often referred to as blunt aortic injury due its clinical and public health significance. Aortic lesions are common outcomes in patients with chest trauma. They are responsible for up to 40% of fatalities occurring in traffic crashes. (Frick et al., 1997; Mirvis et al., 1987; Feczko et al., 1992; Jones, 1970a; Ginzburg et al., 1998a) Studies based on autopsy findings have shown that between 12% and 29% of all traffic fatalities have thoracic aortic traumas. (Parmley et al., 1958b; Feczko et al., 1992; Greendyke, 1966; Shkrum et al., 1999; Stern et al., 1974a; Candell et al., 1979a; Pifarre et al., 1982a; McCabe et al., 1974) Thoracic aortic rupture carries a mortality rate of over 90%, with on-scene death occurring in more than 80% of individuals dying from this injury. (Parmpley et al., 1958b; Feczko et al., 1992; Stern et al., 1974a) In a study by Smith et al., blunt trauma to aorta was found to be the second most common cause of death following head injury. (Smith and Chang, 1986) Parmley noticed that

85% of patients with fatal blunt aortic injury died at the crash scene. (Parmley et al., 1958b) In the US, approximately 7,500 to 8,000 cases of blunt aortic injury occur each year, of which about 1,000 to 1,500 survive long enough to reach a hospital, since as mentioned above, about 85% die at scene. (Smith and Chang, 1986; Parmpley et al., 1958b; Jackson, 1984; Mattox, 1989) Lethality remains very high even after admission to the hospital. In the study conducted by Fabian et al.(Fabian et al., 1988), 274 blunt aortic injury cases were studied during 2.5 years. Motor-vehicle accidents were the leading cause (81%). The lethality was 31% with 63% of deaths due to aortic rupture. Fabian et al.(Fabian et al., 1988) concluded that aortic rupture remains a major problem.

Although severe aortic injuries are largely lethal, minimal aortic injuries, which are defined as a small (<1 cm) intimae flap with no or minimal periaortic hematoma, are also very important. (Ahrar and Smith, 1998; Malhotra et al., 2001; Murray and Lopez, 1997) The potential adverse consequences of not operatively repairing minimal aortic injuries include formation, enlargement, and rupture of pseudoaneurysm; embolism of loose intima, or thrombus and progressive dissection of the aortic wall. (Ahrar and Smith, 1998; Malhotra et al., 2001; Murray and Lopez, 1997)

The main causes of blunt traumatic aortic injuries (76%) are lateral and head on motor vehicle collisions at speeds greater than 50 km/h, or crashes associated with substantial car deformation, followed by a fall from heights - usually exceeding 3 m - and crush injuries. (Williams et al., 1994; Katyal et al., 1997; Fang and Li, 1994; Atalar et al., 2001a; Park et al., 2003a)

Although blunt injury to the cardiovascular system is the major focus of this review, we will briefly mention penetrating vascular and cardiac injury. These injuries usually result from

gun shot or stab wounds with survival rates ranging from 7% to 65%. (Pretre and Chilcott, 1997) Penetrating cardiac trauma frequently accompanied by trauma to lungs, liver and other inner organs. (Pretre and Chilcott, 1997) In the large study which was conducted over 30 years, 4459 patients were found to have 5760 vascular injuries mostly from penetrating mechanisms (all major vessels in the body were identified). (Mattox et al., 1989)

1.1.5.2.   Anatomy and physiology of the human heart

The human heart drives the entire circulatory system. It lies in the mediastinal space within the central area of the thoracic cavity. The heart is surrounded by the pericardium which consists of two layers: the outer (fibrous) layer and the inner (serous) layer. The inner (serous) layer also consists of parietal and visceral portions. The outer layer is attached to other organs and parts of the thoracic cavity (diaphragm, the great vessels and the sternum).

The heart itself consists of three layers. The epicardium is the outer layer that covers the entire heart. The myocardium or the middle layer, is responsible for ventricle pumping. The endocardium, the inner layer of the heart, lines the inner surface of the heart including chordae tendinea and cardiac valves. Chordae tendinea is composed of the tissue that connects the free edges of mitral and tricuspid valves with the papillary muscles. The papillary muscles are connected to the walls of the ventricles.

The heart has four chambers. There are two ventricles and two atria. Blood flows from right atrium to the right ventricle, from the lungs via pulmonary veins into the left atrium and finally into the left ventricle.

The right atrium has the thinnest muscle wall. It receives venous blood from all organs (except lungs) and all four extremities via the superior vena cava, the inferior vena cava and from the coronary sinus. Inspiration causes right atrium pressure to drop below that in the

inferior and superior venae cavae so that blood flows into the right atrium. The average right atrial pressure is about 2 to 6 mm Hg.(Gavaghan, 1998; Shields, 1969) The right atrium is shaped in a such a way that the blood flow is directed toward the right ventricle via the tricuspid valve.

The right ventricle is composed of the body of the right ventricle and the infundibulum. The body of the right ventricle consists of a myocardium, the tricuspid valve, the chordae tendinea and the papillary muscle. The right ventricle ejects blood though the pulmonary (or sometimes called pulmonic) valve into the pulmonary artery. The pulmonary artery then delivers this blood to lungs. The right ventricle wall is about three to five millimeters thick; normal end-diastolic pressure ranges from 0 to 8 mm Hg and normal systolic is 15 to 28 mm Hg. (Gavaghan, 1998; Shields, 1969)

Compared to the right atrium, breathing does not affect left atrium filling. Normal filling pressure is about 8 mm Hg on average. The left atrium has a capacity of approximately 65 ml of blood and pumps into the left ventricle via the mitral valve. (Gavaghan, 1998; Shields, 1969) Compared to other cardiac chambers, the left ventricle has the thickest muscular wall. It ejects blood through the aortic valve to the aorta. The aorta delivers blood to all inner organs, brain and extremities. Normal diastolic pressure is 4 to 12 mm Hg and normal systolic pressure is 90 to 140 mm Hg. (Gavaghan, 1998; Shields, 1969) The right and left ventricle are separated by the ventricular septum, which has electrical conduction tissue.

There are four cardiac valves: mitral, tricuspid, pulmonary and aortic. The mitral valve has two leaflets and is anchored in place by chordae tendinea and papillary muscles. Both leaflets slightly overlap each other when valve is closed. The tricuspid valve is also anchored by chordae

tendinea, however, tricuspid valve has three leaflets. Both aortic and pulmonary valves have three leaflets; however, they do not have the chordae tendinea to anchor them.

Cardiac output is the quantity of blood ejected each minute into aorta by the ventricle. Stroke volume is the amount of blood ejected by the left ventricle with each heart contraction. Stroke volume is affected by preload, afterload and the strength of the ventricular contraction. Preload is determined by the volume in the ventricle before the contraction. Afterload is determined by the vascular resistance and the amount of blood in the left ventricle. The strength of the ventricular contraction is the ratio of blood pumped from the ventricle in one contraction to the ventricle's total capacity.

Both left and right coronary arteries originate from the sinuses of Valsalva just above the aortic valve. Coronary arteries provide the capillaries of the myocardium with blood. The left anterior descending artery and the left circumflex artery are the two main branches of the left coronary artery. The left circumflex artery provides blood to the heart's left posterior side. The left anterior descending artery supplies blood to the left anterior side. The right coronary artery supplies the right atrium, right ventricle and inferior wall of the left ventricle.

The heart has two grooves: the atrioventricular and the interventricular. Both grooves meet on the posterior side of the heart forming the crux of the heart. The important feature of the crux is the atrioventricular node which is nourished by either the right coronary artery or left coronary artery. Left or right dominance is determined by the artery that crosses the crux. Most people are right coronary artery dominant.

Coronary blood flow at rest is about 225 mL per minute. (Gavaghan, 1998; Shields, 1969) It increases three to four times during exercise. Two major factors determine blood flow though the coronary arteries: vascular resistance to flow and driving pressure, which is the

pressure in the aorta minus right atrial pressure. Both sympathetic and parasympathetic divisions of the autonomic nervous system regulate the coronary arteries resulting in either vasoconstriction or vasodilatation, respectively.

The heart's electrical conduction system is composed of nodal cells that can generate and conduct electrical impulses through a series of specialized paths. The initial point of electrical impulse generation is the Sino-Atrial node that causes the heart to beat at a rate of 60 – to 100 beats per minute. (Gavaghan, 1998; Shields, 1969) This node locates above the tricuspid valve. The atrioventricular node is the second major electrical node. It locates near three major cardiac valves: tricuspid, mitral and aortic. This node prodeces a heart rate of 45 to 50 beats per minute. (Gavaghan, 1998; Shields, 1969) Due to this valve anatomical location, it is important to note why damaged or diseased valves can adversely affect the heart's normal electrical pathways often resulting in arrhythmias. The Bundle of His is the third major electrical node and is the only electrical connection between the atria and the ventricles. This node maintains a rhythm of 40 to 45 beats per minute. (Gavaghan, 1998; Shields, 1969) It has two major branches: the right bundle brancj and the left bundle branch. Injury to any of these nodes (the Sino-Atrial, the atrioventricular, the Bundle of His) will result in complete blockage of the conduction pathway distal to the injury.

1.1.5.3. Biomechanics of the chest wall: deceleration and compression

Despite the fact that the heart is "trapped" inside the thorax and protected by the sternum, vertebrae column and ribs, there are several mechanisms that may explain how cardiac tissue may be damaged by external blunt forces. The chest wall is considered to be a viscoelastic tissue that has a certain degree of compliance. This wall may appear to be a relatively stiff tissue when pushed "statically" by hand, for instance during sport related trauma. However, when significant

loads are applied during a motor vehicle crash, the thoracic wall may undergo considerable deformation. If a blunt force is propelled towards the thorax or abdominal wall, a load is applied to the body wall. (Cooper and Taylor, 1989) Due to the significant magnitude of the loads and forces the thoracic wall may be significantly deformed within the area of impact and at the impact site. The primary biomechanical response that is responsible for the transfer of energy into the body and the appearance of the internal injury is the rapid displacement of the abdominal or thoracic wall. (Cooper and Taylor, 1989)

Another issue which needs to be considered is the anteroposterior diameter of the thorax; the narrower the diameter the greater the impact of deceleration or compression. (Cooper and Taylor, 1989) Finally, the reflexes and use of protective gear in athletes or safety features of motor vehicles are very important factors to consider as well. (Cooper and Taylor, 1989)

A deceleration force affects the chest wall and causes either direct pressure on cardiac tissue or indirect compression by increasing intrathoracic pressure and shear stresses. Such indirect compression was consistent with experimental evidence suggesting that a sternal blow can decrease the anteroposterior diameter by 50%. (Kaye and O'Sullivan, 2002) On the other hand, compression of the heart and the aorta between the sternum and vertebral column might result in a left posterior displacement of the heart causing a traumatic ventricular and aortic lesion, sometimes associated with thoracic vertebral fractures. (Ahrar and Smith, 1998)

As mentioned earlier, the external cardiac layer (the pericardium) has loose attachments to the surrounding tissues (sternum and the sternal part of the diaphragm). The heart, therefore, is a relatively unfixed organ and with its weight, retains the potential for a high inertia. Other attachments from the great vessels and their associated fibrous connective tissues are relatively

weak. From a biomechanical point of view, the heart then could be modeled as a chamber filled with fluid tethered and hanging from a fixed point. (Cooper and Taylor, 1989)

Let us assume that the anterior wall of the chest is impacted. If the blow has short duration, the chamber would remain largely stationary. However, the anterior chamber wall would be distorted, which is known as local shear (Cooper and Taylor, 1989) which is more likely to induce injury on the anterior cardiac surface. The right ventricle is most commonly injured because of its anterior position (behind the sternum). When the right ventricle ejection fraction is decreased, the right end diastolic volume is increased, leading to shifting of the intraventricular septum to the left. Even in the absence of direct injury, left ventricular output can decrease due to reduced preload. An injured right ventricle can result in intraventricular septum shift which also contributes to biventricular failure. Up to a 40% decrease in cardiac output can be attributed to the kind of injury and this can persist for several weeks.(Gavaghan, 1998; Shields, 1969)

After the action of the local shears is completed, the transfer of momentum would result in significant motion of the entire chamber away from the impact point with stress of the string suspending it. (Cooper and Taylor, 1989) At this point, the posterior cardiac surface is impacted. Such a mechanism can be also applied to any direct or indirect injury to the heart and great vessels.

This mechanism was studied in detail in anesthetized pigs. Pigs were exposed to impacts to the anterior chest. (Cooper and Taylor, 1989) All impacts were 3.7 sm diameter, 140 gram at velocities ranging from 30 to 64 m/s. Silver spheres were inserted to the cardiac tissue and aorta of pigs at certain anatomical sites whose motion was believed to provide insights on the strains induced under dynamic loading. The swine heart had been compressed to approximately 50% of

its initial anteroposterior dimension within about 4 ms after the projectile was used. Such significant compression resulted in sudden increase of internal pressures within the cardiac chambers. Coronary vessel injury was produced by transfer of the pressure wave from heart chamber down to coronary sinus.

Thus, so far we have shown a few components of the mechanism of cardiac injury. Direct contact of the sternum upon the heart may induce injury on the anterior cardiac surface. The shearing consequence of the ventricular distortion is the primary cause of the injury on the posterior cardiac surface. Compression of the heart is one of the mechanisms of the injury of the coronary vessels. We will review other mechanisms that are involved in the injury to cardiovascular system in more detail below.

1.1.5.4. Indirect forces

Indirect forces are usually associated with sudden compression or crushing of the abdomen or pelvis. In general, sudden compression or crushing of the abdomen or pelvis results in increase of intravascular hydrostatic pressure.(Obadia et al., 1995) Beck and Bright have shown that sudden increase in hypostatic pressure may result in cardiac damage. (Gayet et al., 1987) In addition, cases of combined abdominal trauma and cardiac injury have been reported.(Haas et al., 1968) In two other clinical case studies, a clinical example of cardiac rupture due to indirect force has been reported. (Parmley et al., 1958a) (Gayet et al., 1987) (Rea et al., 1969; Dubrow et al., 1989; Parry and Wilkinson, 1997)

Sudden elevation of intra-aortic pressure caused by sudden external impact to the abdominal area may possibly result in rupture of the coronary vessel particularly if the aortic valve was closed during the traumatic impact (during systole). In a study by Ochsner et al.(Haas et al., 1968; Mayfield and Hurley, 1984; Dubrow et al., 1989; Parry and Wilkinson, 1997) 83%

of aortic ruptures occurred in patients with an anterior-posterior pelvic fracture pattern, and an incidence of aortic rupture was more than 9 times greater in these patients than the incidence of aortic rupture in the overall blunt trauma population (7.5% vs. 0.8; p<0.001).

1.1.5.5. Mechanism of traumatic cardiac valve insufficiency

Various mechanisms have been proposed to describe mitral valve injuries(Stern et al., 1974a): (1) cardiac rupture or subendocardial hemorrhage resulting from a sudden elevated intrathoracic or intra-abdominal pressure; (2) a sudden deceleration or acceleration with secondary thrust of the heart between the sternum or vertebrae; (3) a forceful blow over the sternum with compression of the heart between the sternum or vertebrae.

Acute severe elevation of right intraventricular pressure has been shown to result in injury to the tricuspid valvular apparatus.(Perlroth et al., 1986) Furthermore, the right ventricle is immediately behind the sternum, which makes more vulnerable to blunt trauma.(Banning et al., 1997) Rupture of the valve is more likely to occur if the injury occurred during diastole when the right ventricular pressure is low, particularly when the right ventricle is compressed between the sternum and the vertebrae column.(Bortolotti et al., 1997) The most frequently reported injury is chordal rupture, followed by rupture of the anterior papillary muscle and leaflet tear, primarily of the anterior leaflet.(Perlroth et al., 1986) The right ventricle has also been shown to be vulnerable to indirect injury by a sudden increase in intracardiac pressure from compression of the upper abdomen.(Banning et al., 1997)

The mechanism of "delayed" rupture has been shown to cause traumatic aortic regurgitation, explained by the presence of BCI.(Parry and Wilkinson, 1997) Post-traumatic aortic valve regurgitation has been found to affect all ages and is often found with sternal or multiple rib fractures.(Pretre and Faidutti, 1993) The valve damage is more likely to occur during

systole or early diastole because of compressive forces that may arise following a deceleration injury. At this point in the cardiac pressure and volume cycle, the aortic valve is closed and the transvalvular gradient is maximal.(Pretre and Faidutti, 1993)

We were also interested in describing the mechanism of traumatic valvular disorders. Our previous finding that blunt chest trauma may lead to the appearance of mitral valve dysfunction (Ismailov and Weiss, 2003) correlates with the theoretical research that was explored concurrently.(Ismailov et al., 2003) We attempted to imitate the appearance of mitral valve prolapse resulting from chest trauma. We theorized the appearance of this valve dysfunction may result from a hemodynamic wave. The effect of trauma may be greatly exaggerated if it occurs during the cardiac cycle when valves are closed. Sudden heart displacement as the result of anterior movement of the chest causes accelerated blood flow toward the myocardium and cardiac valves. This wave causes a sudden increase in intracardiac pressure (in the regions where this wave appears) and pushes on the valves causing the extension of their supporting muscles (chordae and papillary muscles). After anterior movement of the chest has been completed, the chest, as the result of rapid deceleration, moves to the posterior direction, that resulting in the appearance of what we call, the "reverse hemodynamic wave". This wave results in increased intracardiac pressure. It pushes on the mitral valve when it is closed, extending what has been already extended by the previous hemodynamic wave and further resulting in prolapsing of the mitral valve.

Our major research finding, after all mathematical equations have been solved, was that additional load or increased air pulse flow created oscillations in the range of 140 – 250 hertz. The diagnosis of MVP was based on the following findings: mid- or late-systolic click, late-systolic murmur or holo-systolic murmur at rest on phonocardiography. The amplitude of such

oscillations ranged between 160 – 190 hertz, i.e. close to the amplitude of oscillations of the pivot-plate in our physical experiment. We concluded that our model quite adequately described the process of appearance of traumatic mitral valve insufficiency.

1.1.5.6. Mechanism of blunt trauma to large vessels

A few mechanisms have been hypothesized to explain blunt lesions in the thoracic aorta. (Atalar et al., 2001a; Sinha et al., 2002; McCabe et al., 1974; Heymann and Culling, 1994a) Sudden lateral or anterior-posterior deceleration has been shown to induce anterior cardiac displacement, leading to injuries of the aortic isthmic level.(Ahrar and Smith, 1998; Shkrum et al., 1999; Katyal et al., 1997; Sinha et al., 2002; McCabe et al., 1974) In injuries caused by a fall, the leading mechanism is a rapid vertical deceleration often resulting in compression against the anterior rib cage and damage to the ascending aorta. (Ahrar and Smith, 1998; Shkrum et al., 1999; Katyal et al., 1997; Sinha et al., 2002; McCabe et al., 1974) Low thoracic or abdominal compression might result in a sudden increase of the intra-aortic pressure often leading to ascending aortic injuries immediately above the aortic valve. (Ahrar and Smith, 1998; Shkrum et al., 1999; Katyal et al., 1997; Sinha et al., 2002; McCabe et al., 1974) Compression of the heart and the aorta between the sternum and vertebral column might result in a left posterior displacement of the heart causing a traumatic aortic lesion, sometimes associated with thoracic vertebral fractures. (Ahrar and Smith, 1998; Shkrum et al., 1999; Katyal et al., 1997; Sinha et al., 2002; McCabe et al., 1974)

Our understanding of the mechanism of blunt trauma to large vessels which takes into account local hemodynamic and rheological factors can be summarized as follows. (Ismailov, 2005) Trauma leads to the appearance of zones with high shear stress (as the result of injury of a part of the vessel) and low or zero shear stress (within the zone of boundary layer separation)

(Konecke et al., 1971). We have reported that high shear stress (i.e. which exceeds the physiological value) may potentially damage the endothelium (Konecke et al., 1971) and also increases platelet aggregation (Mclaughlin et al., 1964; Smedira et al., 1996) leading to thrombus formation. Since trauma may lead to boundary layer separation, this may result in the appearance of a zone with zero shear stress and zero yield velocity (Konecke et al., 1971) and therefore, according to our research findings, in an increase of blood viscosity through increased aggregation of erythrocytes and increased rouleaux formation. (Ismailov, 2005)

1.1.5.7.   Mechanism of blunt injury to the vascular wall: traumatic myocardial infarction

We conducted experiments in an aerodynamic tube, where incident flow velocity and weight of carriage with particles before and after blowing were measured. (Ismailov et al., 2004; Ismailov, 2005) We applied Navier-Stokes, multiphase and boundary layer equations to examine such stress. The method of approximation to solve the boundary layer equations was used. These models of traumatic damage to the vessel that takes into account local rheological and hemodynamic factors could be applied to many internal injuries that involve an elastic vessel wall and a blunt traumatic mechanism.(Ismailov et al., 2004; Ismailov, 2005)

We found that trauma may lead to increased values of shear stress that exceeds physiological value. (Ismailov et al., 2004; Ismailov, 2005) There is evidence that high shear stress may cause endothelial injury.(Fry, 1968) However, the shear stress required to damage the endothelium is far beyond that found in the normal physiological conditions.(Anonymous1978) We found, however, that the value of shear stress is directly related to the value of the force of acceleration that results from injury. Trauma, therefore, due to possible significant compression might cause an increase in the value of shear stress as much as 3-fold. Experimental observations

indicate that platelet aggregation in the myocardial circulation can cause arrhythmias, sudden death, vasculitis, and myocardial ischemic damage.(Moore, 1976)

Our understanding of the mechanism of blunt injury to the vascular wall which takes into account local hemodynamic, rheological factors, rouleaux formation and other factors can be summarized in the following way. The sympathetic nervous system can be "overactivated" by traumatic injury which may result in the excess release of catheholamines. (Moosikasuwan et al., 2000a) These hormones result in increase of heart rate and myocardial oxygen demand. (Moosikasuwan et al., 2000a) Increased blood velocity in such elastic arteries as coronary arteries may lead to increase in shear stress and may also lead to the damage of the endothelium which may further result in thrombus dissection and plaque rupture. (Ismailov et al., 2004) Other factors such as acute coronary spasm, an intimal tear, dissecting aneurysm, coronary embolism and subintimal hemorrhage have been also shown to be contributing mechanisms. (Lee et al., 1991a; Chun et al., 1998a) Based on our findings, blunt trauma may result in the appearance of a region of very low or zero shear stress, where hyperviscosity and increased rouleaux formation are likely to appear. (Ismailov et al., 2004; Ismailov, 2005) Large quantities of rouleaux may be transported in bloodstream toward the more distal parts of coronary vessels causing their occlusion. (Ismailov et al., 2004; Ismailov, 2005) Caimi et al. (Mach et al., 1995), for instance, have observed that at a low shear rate, blood viscosity is the only hemorheological factor that significantly increases the risk of acute myocardial infarction in young people.

On the other hand, blunt trauma may result in the appearance of traumatic compression of the vessel wall with high shear stress (Konecke et al., 1971). Increased shear stress itself may cause the rupture of coronary atherosclerotic plaque(Parry and Wilkinson, 1997). In addition,

high shear stress may result in increased platelet aggregation (Mclaughlin et al., 1964; Smedira et al., 1996) often leading to thrombus formation.

1.1.5.8. Mechanism of traumatic cardiac arrhythmias

Several mechanisms have been hypothesized to explain cardiac arrhythmias and conduction abnormalities resulting from trauma including abnormal perfusion patterns, vagal sympathetic reflex and abberant conduction by damaged myocardial cells.(Darok et al., 2001a) Conduction abnormalities usually result from intramyocardial hemorrhage into conduction tissue.(Brennan et al., 1979) They may also result from excessive excitation of cholinergic reflexes. (Brennan et al., 1979) (Gertz and Roberts, 1990) The mechanism of traumatic cardiac arrhythmias was studied in animals. Schlomka conducted a series of experiments where he traumatized the heart by direct blows. Both ventricular tachycardia and fibrillation were observed. (Parmley et al., 1958a) Link et al.(Link et al., 1998) conducted a series of low energy impacts to the chest wall in a swine model. Researchers concluded that the risk and type of arrhythmia depend on when the impact occurred during the cardiac electric cycle. (Link et al., 1998) Evidence that cardiac arrhythmias may result from relatively 'mild' sport traumas perhaps suggesting that the strength of the impact is less important has been also introduced by various researchers who noticed that various types of arrhythmias may appear from usually innocent-appearing chest blows in various sport activities.(Wallen et al., 1995)

Therefore, the risk of cardiac arrhythmia is directly proportional to both the force and speed of the impact and inversely proportional to the size of the contact area. On the other hand using the swine model it was shown that even low energy impact can have immediate and significant effect if applied during a short and vulnerable time interval (i.e. upstroke of the T

wave) resulting in ventricular fibrillation. Complete heart block and left bundle –brunch block were produced by impacts during the QRS complex.

1.1.6.   Blunt cardiac injury

BCI, also formerly known as "cardiac" or "myocardial" contusion, is defined as myocardial cellular damage that usually results from blunt chest trauma. (Parmley et al., 1958a)

1.1.6.1.   Epidemiology

The true incidence of BCI is difficult to estimate due to lack of standard diagnostic methods. Nevertheless, BCI has been described as the most frequent cardiac injury following blunt chest trauma and occurs in 16% to 76% of patients involved in motor vehicular accidents. (Tenzer, 1985)

In a few autopsy and clinical case studies, the incidence varies from 10% to 75% in the presence of severe trauma or chest injury. (Leinoff, 1940; Osborn, 1943; Sigler. L.H., 1945) Subsequently, Lindstaedt et al.(Lindstaedt et al., 2002) attempted to estimate the incidence of BCI by looking at patients admitted to the surgical intensive care unit. Among all trauma patients admitted to the intensive care unit, an incidence of 19.4 was found. (Lindstaedt et al., 2002)

Incidence of BCI also varies depending on the diagnostic approach. Despite several studies, no consensus on a standard diagnostic approach to evaluate BCI has been reached. Advantages and disadvantages of various diagnostic techniques have been summarized below (see table 1). Low incidence of BCI was found in a study where the cardiospecific enzymes were used yielding 19%.(Helling et al., 1989) Low incidence of BCI varying between 3 and 26% of patients with blunt chest trauma were also found in transthoracic echocardiography studies.(Bertinchant et al., 2000; Karalis et al., 1994; Illig et al., 1991; Helling et al., 1989; Hiatt

et al., 1988; Salim et al., 2001; Frazee et al., 1986b; Adams et al., 1996; Collins et al., 2001) Incidences were higher when a transesophageal approach was used so that BCI was detected in 27-56% of the patients.(Karalis et al., 1994; Brooks et al., 1992; Weiss et al., 1996; Garcia-Fernandez et al., 1998) High incidences, however, were also found in ECG studies of patients with blunt chest trauma ranging from 29% to 56%. (Bertinchant et al., 2000; Illig et al., 1991; Helling et al., 1989; Hiatt et al., 1988; Salim et al., 2001) Finally, using highly specific troponin I or T, incidences of BCI varied from 15% to 24%. (Salim et al., 2001; Adams et al., 1996; Collins et al., 2001)

We were also interested in the post-injury functional state of the cardiovascular system among healthy adults. In previous studies, patients have been shown to have various cardiovascular abnormalities detected by various diagnostic tests. (Ginzburg et al., 1998a; Tenzer, 1985; Nagy et al., 2001; Bertinchant et al., 2000; Keller and Shatney, 1988) However, clear evidence of presence or absence of such abnormalities before the episode of chest trauma was not always clearly established. This could potentially result in overestimation of BCI prevalence, particularly among elderly people. We investigated 200 injured male military recruits (mean age 19.4 years) suffering non-severe blunt chest trauma, with no history of previous cardiovascular disease. (Ismailov and Weiss, 2003) Each prospective male military recruit previously underwent an admission process at age 18 which included a baseline multiple stage health examination process performed by medical specialists. Therefore, all study participants had a documented history of absence of cardiovascular disease prior to the episode of blunt chest trauma. Study subjects were investigated using Electrocardiography and Echocardiography at the baseline (24 hours – 7 days subsequent to trauma) and re-investigated using both tests in the follow-up period (3, 6 and 12 months). We divided ECG abnormalities

into three groups: (1) repolarization abnormalities; (2) arrhythmias; (3) conduction abnormalities. We also divided abnormalities found on echocardiography into two groups: (1) deterioration in LV global or/and regional systolic abnormalities; (2) Mitral valve dysfunction. Of the 200 subjects, 61% were found to have abnormal valvular function and/or abnormal left ventricular function within 7 days subsequent to trauma and 28.5% of the subjects were found to have one or more cardiac symptoms over the 12 months of follow-up. At baseline, the most prevalent ECG abnormality in our study was the group of repolarization abnormalities (47%) following by arrhythmias (30%). Repolarization abnormalities as a group remained the most prevalent in 3, 6 and 12 months. Abnormal global and/or regional systolic LV function was more prevalent at the baseline (25%); however, the mitral valve dysfunction group was more prevalent in all follow-up periods (16%, 16% and 15% prospectively).

Table 1 Diagnostic techniques for blunt cardiac injury

Diagnostic test	Advantages	Disadvantages
CPK-MB isoenzymes	A CK-MB concentration of 200 mg/dL or greater may have a 100% positive predictive value for cardiac complications. (Healey et al., 1990)	Many false positive results were found in mutlitraumatized patients. (Frazee et al., 1986a; Tenzer, 1985) Both low sensitivity and specificity of CK-MB for cardiac injury were reported among mildly injured patients. (Bertinchant et al., 2000; Nagy et al., 2001; Keller and Shatney, 1988)
ECG	Appears to have an excellent negative predictive value for cardiac complications. (Healey et al., 1990; Dubrow et al., 1989; Foil et al., 1990)	Results are nonspecific. (Potkin et al., 1982; Mooney et al., 1988)

Table 1 (continued) Diagnostic techniques for blunt cardiac injury

Radionuclide angiography	May rule out ventricular aneurism and may identify cardiac sources of hemodynamic instability. (Fenner et al., 1984) Sensitive in detecting an isolated trauma to the right ventricle. (Sutherland et al., 1983)	No more accurate than cardiac enzymes and ECG for determining the presence of serious cardiac injury (Olsovsky MR 1997)
Transthoracic two-dimensional echocardiography	May identify and assess effusions, myocardial contractility, regional wall motion, aneurysms, intracardiac shunts, and valve integrity. (Cho et al., 1995)	Less effective as a screening tool for cardiac contusion since approximately 25% of trauma patients can not be satisfactory imaged. (Karalis et al., 1994) It provides little information in hemodynamically stable patients. (Karalis et al., 1994; Fabian et al., 1988; Christensen and Sutton, 1993)
Transesophageal echocardiography	More sensitive in detecting BCI than transthoracic two-dimensional echocardiography. (Karalis et al., 1994; Brooks et al., 1992) Useful for diagnosis of traumatic aortic dissection. (Olsovsky et al., 1997)	Requires certain operator skill and experience. (Olsovsky et al., 1997)
Cardiac troponin T (cTT)	A highly specific and sensitive marker for myocardial cell damage. (Mach et al., 1995)	Will be elevated by trauma to cardiac tissue possibly masking presence of combination of myocardial infarction and BCI. (Olsovsky et al., 1997)

1.1.6.2. Clinical symptoms

Clinical signs of BCI may appear during the first hours after trauma (shortness of breath,

weakness, tachycardia, cardiac pain of various character. (Anonymous1991) Pain might develop

as a sense of constraint inside the chest; sometimes pain becomes stronger during deep breathing

or during palpation of the chest. (Anonymous1991) A patient may not have signs of injured chest on examination. (Anonymous1991)

1.1.6.3. Classification

There are three periods in BCI development. (Anonymous1991)

I – Acute period (lasts 2-3 days).

During this period cardiac muscle might decrease its tonus. Areas of local failure of kinetics of myocardium and hypoxia can be diagnosed by electrocardiogram while decrease of contracting function of ventricles of the heart can be observed on echocardiography. Acute cardiac failure may eventually develop. (Anonymous1991)

П – Period of regeneration (lasts up to 12-13 days).

During this period cardiac dystrophy might develop and phenomena of necrosis of injured muscle fibers prevail. This recovery period is characterized by gradual standardization of cardiac hemodynamics.(Anonymous1991)

Ш – Period of posttraumatic cardiosclerosis that begins after 14 days and can have durable term.

Clinical symptoms are characterized by slow reverse development. (Anonymous1991) Standardization of electrocardiogram changes might last for 4-6 weeks. (Anonymous1991)

1.1.6.4. Treatment

Treatment is directed to recovery of functions of the injured heart and is conducted differentially depending on the period and criticality of disease. Patients with BCI should be treated under a cardiologist's observation.(Anonymous1991) Therapy should have an individual complex approach depending on the severity of accompanying injuries and character of hemodynamical failures. Treatment is directed toward standardization of arterial pressure, elimination of rhythm and conduction failure.

1.2. BLUNT CARDIAC INJURY ASSOCIATED WITH CARDIAC VALVE INSUFFICIENCY: TRAUMA LINKS TO CHRONIC DISEASE?

Cases of mitral valve (Cho et al., 1995; Anyanwu, 1976a; Bailey et al., 1969; Bryant et al., 1973a; Devineni and McKenzie, 1983; Manhas et al., 1971; McCrory et al., 1991; Mclaughlin et al., 1964; Wilke et al., 1997; Gomez and Jackson, 1966; Szakacs, 1966; Harada et al., 1977; Bruschi et al., 2001; Cuadros et al., 1984; Goetz et al., 2001; Grinberg et al., 1998; Kugai and Chibana, 2000; Rashid et al., 1978; Reardon et al., 1998; Van Roye and Zienkowicz, 1989), aortic valve(Parry and Wilkinson, 1997; Obadia et al., 1995; O'Connor and Davis, 1980; Mccormack and Proudfit, 1956; Pretre and Faidutti, 1993; Chi et al., 1977; Levine et al., 1962; Beall and Shirkey, 1964; Lutes and Givertz, 1970; Loop et al., 1971; Cleveland and Cleveland, 1974; Charles et al., 1977; McIlduff and Foster, 1978) and tricuspid valve(van Son and Starr, 1995; Gayet et al., 1987; Banning et al., 1997; Bortolotti et al., 1997; Perlroth et al., 1986; Dounis et al., 2002; Katz and Pallas, ; Brandenburg et al., 1966; Jahnke et al., 1967; Shabetai et al., 1969; Cahill et al., 1972; Stephenson et al., 1979) injury have been described in the literature. None of the studies described pulmonary valve injury. Most of these cases followed by rupture or damage to the papillary muscles, rupture of chordae tendinea and / or rupture or laceration of the valve leaflet. Motor vehicle crashes were found to be the major reported cause of traumatic valvular injury (Bailey et al., 1969; Bryant et al., 1973a; Devineni and McKenzie, 1983; Mclaughlin et al., 1964; Harada et al., 1977; Cuadros et al., 1984; Goggin et al., 1970; Mazzucco et al., 1983; Munim and Chodoff, 1983; Pellegrini et al., 1986; Al Kasab et al., 1988; Fiane and Lindberg, 1993; Spangenthal et al., 1993; Coleman et al., 1994). Other causes included falls (from horse, truck or roof) (Anyanwu, 1976a) (Manhas et al., 1971) (Rashid et al., 1978)and struck by metal bar. (Pillai et al., 1982) The time interval between exposure to injury or the

diagnosis and surgical correction ranged from several hours (Kratz et al., 1980; Munim and Chodoff, 1983) to several days (Bryant et al., 1973a; Pillai et al., 1982; Pellegrini et al., 1986; Chang et al., 1989b; Coleman et al., 1994) and even months. (Bailey et al., 1969; Weldon et al., 1972)

Most patients underwent valve replacement (Anyanwu, 1976a; Bryant et al., 1973a; Rashid et al., 1978; Pillai et al., 1982; Pellegrini et al., 1986; Al Kasab et al., 1988; Werne et al., 1989; Fiane and Lindberg, 1993). In some patients papillary muscle was re-inserted and these patients further underwent annuloplasty. (Chang et al., 1989b; Coleman et al., 1994; McDonald et al., 1996) The majority of patients were reported to survive after surgical treatment and only in two cases surgical intervention was not successful. (Mclaughlin et al., 1964; Munim and Chodoff, 1983)

1.3.   TRAUMA ASSOCIATED WITH ACUTE MYOCARDIAL INFARCTION: OVERVIEW OF TRAUMATIC MYOCARDIAL INFARCTION

Myocardial infarction (MI) is the major cause of death in the US: about 225,000 people die annually from MI of whom 125,000 die before obtaining medical care. Myocardial infarction has been described as a complication of blunt trauma. (Shapiro et al., 1994a; Vlay et al., 1980a; Lehmus et al., 1954a; Harthorne et al., 1967a; Stewart, 1967a; Rab, 1969a; Jones, 1970a; Ginzburg et al., 1998a; Fu et al., 1999; Fang and Li, 1994; Atalar et al., 2001a; Park et al., 2003a; Lee et al., 1991a; Heymann and Culling, 1994a; Stern et al., 1974a; Candell et al., 1979a; O'Neill et al., 1981; Pifarre et al., 1982a; Watt and Stephens, 1986; Jokl and Greenstein, 1944; Pringle and Davidson, 1987a; Kahn and Buda, 1987a; Boland et al., 1988a; Foussas et al., 1989a; Oliva et al., 1979a; Heyndrickx et al., 1974a; Oren et al., 1976a; Tsagaris and Hecht, 1962; Haas et al., 1968; Rea et al., 1969; Forker and Morgan, 1971; Konecke et al., 1971; Lynn and Fay, 1971;

Morgan et al., 1972; Cheng and Adkins, 1973; Liberthson et al., 1973; Tector et al., 1973; Gaspard et al., 1983a; Goulah et al., 1988; Kohli et al., 1988a; Unterberg et al., 1989a; de Feyter and Roos, 1977a; Motro et al., 1981a; Espinosa et al., 1985a; Lascault et al., 1986a) Motor vehicle accidents were found to be the most common mechanism(Shapiro et al., 1994a; Vlay et al., 1980a; Lehmus et al., 1954a; Rab, 1969a; Ginzburg et al., 1998a; Fu et al., 1999; Lee et al., 1991a; Sinha et al., 2002; Stern et al., 1974a; Candell et al., 1979a; Pifarre et al., 1982a; Pringle and Davidson, 1987a; Kahn and Buda, 1987a; Boland et al., 1988a; Foussas et al., 1989a; Oliva et al., 1979a; Heyndrickx et al., 1974a; Gaspard et al., 1983a; Goulah et al., 1988; Kohli et al., 1988a; Unterberg et al., 1989a), following by sport trauma(Rab, 1969a; Atalar et al., 2001a; Murray and Lopez, 1997; O'Neill et al., 1981; Watt and Stephens, 1986; Jokl and Greenstein, 1944; Oren et al., 1976a; de Feyter and Roos, 1977a; Motro et al., 1981a; Espinosa et al., 1985a) and motor cycle accident.(Fu et al., 1999; Fang and Li, 1994; Park et al., 2003a; Heymann and Culling, 1994a) Unusual mechanisms included falls from height (Foussas et al., 1989a; Lascault et al., 1986a), barroom brawl (Harthorne et al., 1967a), wood from circular saw (Stewart, 1967a) and swept from horse by tree limb (Jones, 1970a).

The left anterior descending artery is the most frequently injured vessel. (Ginzburg et al., 1998a) The less frequently injured vessels are the right coronary and the circumflex coronary arteries.(Park et al., 2003a) Time between trauma and acute myocardial infarction ranged in most clinical reports from a few minutes to several days. Although acute myocardial infarction was found to be a rare complication of trauma, factors such as posttraumatic shock, administration of pain relievers, attention to fluid management and intensive physical therapy may potentially obscure the clinical picture of infarction. (Moosikasuwan et al., 2000a).

Autopsy findings were performed in a few patients. (Lehmus et al., 1954a; Stewart, 1967a; Jones, 1970a; Jokl and Greenstein, 1944; Macdonald et al., 1981) Results from angiographic testing were available in some of the case reports. (Vlay et al., 1980a; Harthorne et al., 1967a; Stern et al., 1974a; Candell et al., 1979a; Pringle and Davidson, 1987a; Kahn and Buda, 1987a; Oliva et al., 1979a; Oren et al., 1976a; Gaspard et al., 1983a; Goulah et al., 1988; de Feyter and Roos, 1977a)

Various forms of myocardial infarction have been reported: anteroseptal (Candell et al., 1979a), anterior (Vlay et al., 1980a; de Feyter and Roos, 1977a), posteriolateral (Stewart, 1967a) and inferior. (Harthorne et al., 1967a; Candell et al., 1979a; Oliva et al., 1979a; Heyndrickx et al., 1974a) In some cases, traumatic myocardial infarction was complicated by right bundle branch block (Vlay et al., 1980a; Stewart, 1967a; Stern et al., 1974a) or complete heart block. (Candell et al., 1979a; Heyndrickx et al., 1974a) Some victims were presented with extensive atherosclerotic coronary artery disease (Lehmus et al., 1954a) while others with insignificant (Stewart, 1967a; Jokl and Greenstein, 1944; Heyndrickx et al., 1974a) and even without any evidence of atherosclerotic CAD. (Candell et al., 1979a; Oliva et al., 1979a; Oren et al., 1976a; de Feyter and Roos, 1977a)

1.4. TRAUMA ASSOCIATED WITH CARDIAC ARRHYTHMIA. OVERVIEW OF TRAUMATIC CARDIAC ARRHYTMIA.

Atrial fibrillation is also one of the most common cardiac arrhythmias encountered in clinical practice.(Prystowsky et al., 1996; Wolf et al., 1991; Longstreth et al., 2001) The prevalence of atrial fibrillation is 0.5% for the group aged 50 to 59 years, approximately 5% if estimated on a 24-hour electrocardiographic recording among people 65 years and older, and rises to 8.8% in the group aged 80 to 89 years.(Prystowsky et al., 1996) Although a major cause of atrial

fibrillation is chronic cardiovascular conditions such as ischemic heart disease or rheumatic disease, in about 10% of people with atrial fibrillation, the "true" cause is unknown.(Fuster et al., 2001; Stollberger et al., 2004)

Cardiac arrhythmias have been frequently reported as a complication of chest trauma. (Mayfield and Hurley, 1984) (Healey et al., 1990; Parmley et al., 1958a; Potkin et al., 1982; Grech et al., 1992; Pontillo et al., 1994; Morikawa et al., 1996; Saranchak and Johnson, 1980; Berk, 1987; Bertinchant et al., 2000; Potkin et al., 1982; Foil et al., 1990; Olsovsky et al., 1997; Wisner et al., 1990; Utley et al., 1976; Finn and Byrum, 1988; Doty et al., 1974; Jones et al., 1975; Harley et al., 1984; Silverman et al., 1990; Sakka et al., 2000; Harrahill, 2004; Vogler and Seaberg, 2001; Brokhes, 1970; Weisz et al., 1976; Grech et al., 1992; Singer et al., 1998; Ellis and Hutchinson, 2000; Fulda et al., 1997; Beresky et al., 1988; McLean et al., 1991; van Wijngaarden et al., 1997; Norton et al., 1990; Cachecho et al., 1992; Fabian et al., 1991; Rosenthal and Ellis, 1995) Such trauma has been shown to produce various types of arrhythmias such as ventricular extrasystoles, atrial fibrillation, supraventricular tachycardia and supraventricular extrasystoles (Bertinchant et al., 2000; Potkin et al., 1982; Foil et al., 1990; Olsovsky et al., 1997; Wisner et al., 1990; Utley et al., 1976; Finn and Byrum, 1988; Doty et al., 1974; Jones et al., 1975; Harley et al., 1984; Silverman et al., 1990; Sakka et al., 2000; Harrahill, 2004; Vogler and Seaberg, 2001; Brokhes, 1970; Weisz et al., 1976; Grech et al., 1992; Singer et al., 1998; Ellis and Hutchinson, 2000; Fulda et al., 1997; Beresky et al., 1988; McLean et al., 1991; van Wijngaarden et al., 1997; Norton et al., 1990; Cachecho et al., 1992; Fabian et al., 1991; Rosenthal and Ellis, 1995) (Parmley et al., 1958a; Potkin et al., 1982; Grech et al., 1992; Pontillo et al., 1994; Morikawa et al., 1996; Saranchak and Johnson, 1980; Berk, 1987) According to some researchers, atrial fibrillation was found to be the most common form of

arrhythmia that presents after trauma. (Healey et al., 1990; Olsovsky et al., 1997; van Wijngaarden et al., 1997; Norton et al., 1990; Cachecho et al., 1992; Fabian et al., 1991) According to Sakka et al(Sakka et al., 2000), uniform ventricular premature beats are the most common type of cardiac arrhythmia resulting from trauma, accounting for 54%, followed by multifocal ventricular premature beats (16%), atrial fibrillation (6%), and ventricular tachycardia (3%).

Traumatic cardiac arrhythmias usually develop within the first hours following injury.(Mayfield and Hurley, 1984; Harley et al., 1984) In some studies, cardiac arrhythmia developed within 24-48 hours after trauma.(Illig et al., 1991; Wisner et al., 1990; Silverman et al., 1990; Norton et al., 1990) According to Sakka et al.(Sakka et al., 2000), patients with blunt chest trauma may experience life-threatening arrhythmias even after several days after trauma.

As mentioned earlier, most traumatic cardiac arrhythmias are transitory conditions that are usually represented as changes in ST-T complex or as right bundle branch block on ECG. Some traumatic cardiac arrhythmias such as ventricular fibrillation may lead to immediate death. A few traumatic cardiac arrhythmias and conduction abnormalities such as atrial fibrillation or paroxysmal ventricular tachycardia, however, may be of clinical importance. Atrial fibrillation is an important risk factor for stroke. The attributable risk is about 1.5% for those aged 50-59 years and almost 30% for those aged 80-89 years. (Stollberger et al., 2004)

Patients with chest injury, therefore, might benefit from certain screening procedures for atrial fibrillation and paroxysmal ventricular tachycardia such as ECG, (Wolf et al., 1991; Longstreth et al., 2001) although normal ECG on admission and during 24 hours in ICU does not exclude fatal cardiac arrhythmias after discharge. (Sakka et al., 2000)

1.5. SPECIFIC AIMS AND HYPOTHESES

Three specific aims of this association are:

1. To evaluate the association between BCI and cardiac valve insufficiency at the population level.

We hypothesize that BCI is significantly associated with insufficiency of certain cardiac valves. To examine this issue, we conducted a cross-sectional analysis of the association between BCI and cardiac valve insufficiency based on a large database of all hospital discharges from 19 states during a one-year period.

2. To evaluate the association between certain types of trauma (blunt cardiac, thoracic, abdominal, pelvic, back and spine) and acute myocardial infarction at the population level

We hypothesize that certain types of hospitalized trauma (thoracic, abdominal/pelvic, spine/back or blunt cardiac injury (BCI), formerly known as myocardial contusion, are associated with increased risk of AMI. To test this hypothesis, we conducted a cross-sectional study of the association between trauma and AMI based on a database of all hospital discharges from 19 states during a one-year period.

3. To evaluate the association between thoracic injury and cardiac arrhythmias at the population level.

We hypothesize that thoracic injury is significantly associated with cardiac arrhythmias. To test this hypothesis we conducted a matched case-control study of the association between trauma and cardiac arrhythmias based on a database of all hospital discharges from 33 states during a one-year period

1.6. PUBLIC HEALTH SIGNIFICANCE

Evidence from multiple clinical case studies suggests that trauma may lead to various cardiovascular disorders such as cardiac valve disorders, myocardial infarction and cardiac arrhythmias. Although the mechanism for such a relationship has been studied, there are no population based studies. It is important, however, to show that trauma may lead to certain cardiovascular disorders. An increasing number of motor-vehicles will likely result in an increased number of motor vehicle crashes and, therefore, the number of blunt thoracic injuries. Approximately 25% of injuries in motor vehicle accidents involve the chest. On the other hand, more than 60% of major chest trauma cases are related to motor vehicle accidents.

Currently, among persons 6 to 27 years, motor vehicle accidents are the leading cause of death. More people are injured and survive motor vehicle accidents than die: 40,000 persons die because of motor vehicle accidents while about 5 million persons are injured on the nation's highways. On the other hand, the number of blunt thoracic injuries in the US has been estimated at 12 per million per day or approximately 100,000 cases per year. Because blunt thoracic injuries are the leading cause of cardiac trauma, the latter will likely to occur more frequently.

Further development of diagnostic tests will improve the detection of latent and mild forms of cardiac trauma. Studies that focus on the diagnosis of cardiac trauma will likely identify the best combination of diagnostic tests to diagnose BCI or the "gold standard" to diagnose this type of injury. Improved diagnosis will also help to prevent various complications that may occur due to "delayed" diagnosis of traumatic cardiovascular events (i.e. ventricular fibrillation due to "delayed" diagnosis of traumatic myocardial infarction).

Cardiovascular diseases are the leading cause of mortality worldwide including the US accounting for nearly 40% of all deaths. Over 930,000 Americans die of cardiovascular disease

each year, which amounts to one death every 34 seconds. Over 64 million Americans (almost one-fourth of the population) live with cardiovascular disease.

It is asserted, therefore, that some traumatic events should be seen as potentially modifiable risk factors for some acute and chronic cardiovascular conditions. By extension, part of the burden of acute and chronic cardiovascular diseases in the population may have its roots in acute injury. If this concept is more widely accepted, it opens up several paths to pursue. One of these is to conduct longitudinal studies of cardiovascular diseases and other chronic conditions to substantiate and better quantify these links. In this manner, the "true" impact of injury in the population will become clearer.

2. ARTICLE ONE: BLUNT CARDIAC INJURY ASSOCIATED WITH CARDIAC VALVE INSUFFICIENCY: TRAUMA LINKS TO CHRONIC DISEASE?

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2.1. ABSTRACT

Context. Cardiac injury has been well recognized as a complication of blunt chest trauma. Its clinical spectrum ranges from blunt cardiac injury (BCI) to complete rupture of cardiac tissues, with cardiac valvular injury often being overlooked.

Objective. To determine whether hospitalized BCI is associated with increased risk of cardiac valve insufficiency in a large multi-state hospitalized population.

Methods. Cases with BCI and cardiac valve insufficiency were identified based on discharge diagnoses in 1997 statewide hospital discharge data from 19 states. Four valvular outcomes were studied: (1) mitral valve insufficiency, incompetence, regurgitation (MVIIR); (2) aortic valve insufficiency, incompetence, regurgitation, stenosis (AVIIRS); (3) tricuspid valve insufficiency, incompetence, regurgitation, stenosis (TVIIRS); and (4) pulmonary valve insufficiency, incompetence, regurgitation, stenosis (PVIIRS).

Results. Among 1,051,081 injury discharges, 2,709 (0.26%) people had BCI; 13,087 (1.25%) had MVIIR; 9,811 (0.93%) had AVIIRS; 1,338 (0.13%) had TVIIRS; 178 (0.02%) had PVIIRS. Independent of potential confounding factors, discharge for BCI was associated with a 12-fold increased risk for TVIIRS and a 3.4-fold increased risk for AVIIRS.

Conclusion. Cardiac valve insufficiency has been well recognized as an important risk factor for congestive heart failure. With the findings that BCI is associated with an increased risk of specific valvular disorders, it is possible that trauma may play an important and heretofore largely unrecognized role in a portion of the burden of cardiovascular morbidity and mortality.

2.2. KEY WORDS

trauma; injury; blunt cardiac injury; cardiac valvular disorder

2.3. ABBREVIATIONS

AVIIRS, aortic valve incompetence, insufficiency, regurgitation, stenosis; BCI, blunt cardiac injury; MAISS, maximum abbreviated injury severity score; MVIIR, mitral valve incompetence, insufficiency, regurgitation; MVT, motor vehicle transportation; N/A, not applicable; PVIIRS, pulmonary valve incompetence, insufficiency, regurgitation, stenosis; SD, standard deviation; TVIIRS, tricuspid valve incompetence, insufficiency, regurgitation, stenosis

2.4. INTRODUCTION

Blunt thoracic trauma may result from motor vehicle crashes, sporting activity, assaults, and falls. In the United States, thoracic trauma accounts for at least 25% of all trauma deaths.[29] Blunt cardiac injury (formerly known as "myocardial contusion"), following blunt thoracic trauma has been described as the most common yet unsuspected visceral injury causing death in injured victims [6,46]

The clinical significance of BCI remains unknown.[33] In those patients with cardiac trauma who reach the hospital alive, however, the greatest contributor to fatality was found to be BCI[54] and there is research that this is due to incomplete diagnosis and assessment.[43] For instance, life-threatening ventricular arrhythmias as a complication of BCI were described in up to 16% of patients with blunt thoracic trauma.[55]

BCI can be characterized by patchy areas of muscle necrosis and hemorrhagic infiltrate, rupture of small vessels, hemorrhage into the interstitium and around the muscle fibers.[12,36,45,46] Such patchy and irregular myocardial cell necrosis can be well recognized at surgery or autopsy but not with conventional imaging studies.[46] The magnitude of BCI itself may vary from absence of any clinical symptoms to complete rupture of cardiac tissues with

sudden death.[3,46,55-57] Patients with BCI might sustain certain intracardiac lesions that are in the middle of this spectrum, but still compatible with survival.

Currently, the primary clinical significance of BCI lies in its effects on the heart itself and the great vessels, with cardiac valvular injury, which has been recognized as a common clinical problem, often being overlooked.[43] Specifically, aortic and mitral valve damage has been recognized as a complication of non-penetrating chest injury [41,42]Most patients with traumatic rupture of the aortic valve suffer it immediately after the initial trauma; however, "delayed" rupture may occur after BCI.[43] Traumatic tricuspid insufficiency is a rarer lesion, although, its frequency is thought to be underestimated.[19]

The objective of this research is to explore whether BCI is associated with increased risk of cardiac valve insufficiency. We hypothesize that BCI is significantly associated with insufficiency of certain cardiac valves. To examine this issue, we conducted a cross-sectional analysis of the association between BCI and cardiac valve insufficiency based on a large database of all hospital discharges from 19 states during a one-year period.

2.5. METHODS

Hospital discharge data were collected from 19 states (Arizona, California, Florida, Massachusetts, Maryland, Maine, Michigan, Nebraska, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, South Carolina, Utah, Virginia, Vermont, Washington, and Wisconsin). Information was obtained for all trauma admissions in 1997 based on ICD-9-CM classification (codes 800-959). The combined 19-state dataset had 1.049 million injury cases, of which 0.967 million were acute. These were drawn from a total of about 17.8 million hospitalizations. This dataset has fields for 15 diagnoses and 6 E-codes, however, the number of diagnosis fields provided by the states ranged from 7 (Rhode Island) to 25 (California).

Extensive editing, filtering and grouping were applied to the data. [58] Derived variables were developed to enhance coding validity, and usability.[58]

Diagnosis codes representing injuries (codes 800-959) were categorized into subgroups based on injury mechanism and intent. The mechanism of injury and its associated intent were classified on the basis of the External Cause of Injury codes, defined within ICD-9-CM.

MVIIR was identified based on ICD-9-CM (424.0), that excludes mitral valve disease (394.9), mitral valve failure (394.9) and mitral valve stenosis (394.0). It also excludes the following conditions: specified as rheumatic (394.1), unspecified as to cause but with mention of diseases of aortic valve (396.0-396.9), and mitral stenosis or obstruction (394.2). AVIIRS was identified based on ICD-9-CM (424.1), that excludes hypertrophic subaortic stenosis (425.1), rheumatic (395.0-395.9) and that of unspecified cause but with mention of diseases of mitral valve (396.0-396.9). TVIIRS was identified based on ICD-9-CM (424.2), that excludes rheumatic tricuspid valve incompetence, insufficiency, regurgitation and stenosis or of unspecified cause (397.0). PVIIRS was identified based on ICD-9-CM (424.3). This diagnosis excludes rheumatic pulmonary valve incompetence, insufficiency, regurgitation and stenosis (397.1). Bacterial or syphilitic valve insufficiency were excluded since "other diseases of endocardium" (ICD-9 code 424) excludes bacterial endocarditis (421.0-421.9), rheumatic endocarditis (391.1, 394.0-397.9) and syphilitic endocarditis (093.20-093.24). BCI was identified based on ICD-9-CM (861.01).

Age has been shown to significantly influence the prevalence of valve regurgitation. [51] Singh et al.[51] found that the prevalence of mitral regurgitation, tricuspid regurgitation, and aortic regurgitation increased with age and are consistent with earlier Doppler studies.[2,8,32] Although left-sided valves (aortic and mitral) are exposed to higher pressures and are likely to

undergo degenerative changes earlier than right-sided valves, prevalence rates of mitral and tricuspid regurgitation have been shown to be comparable at all ages.[32]

Some degenerative conditions (myxomatous degeneration and mitral annulus calcification) have been shown to cause MVIIR and AVIIRS [53], however these conditions do not have ICD-9-CM codes. Since age was shown to dramatically influence degenerative conditions,[53] age was an adjustment factor in all regression analyses.

Ischemic heart disease has been shown to cause MVIIR and AVIIRS.[28] Therefore, ischemic heart disease was identified based on ICD-9-CM (410-414) and was further entered as a covariate in regression analysis for MVIIR and AVIIRS.

Population estimates for states by age, race, sex were identified from "Population Estimates" Program, Population Division, U.S. Census Bureau, Washington, DC 20233, available at: http://www.census.gov/population/estimates/state/sasrh/sasrh97.txt Statistical analysis was conducted using SPSS 11 for Windows. (SPSS, Inc., Chicago, IL). Univariate analysis was performed with Chi-square testing and Fisher exact testing for certain categorical variables (BCI, MVIIR, AVIIRS, TVIIRS, PVIIRS).

All analyses were adjusted for age (10 year age strata), gender (males versus females), race (whites versus non-whites), presence of BCI (yes versus no), maximum abbreviated injury severity score (MAISS) (6 levels, the lowest being "0" and the highest being "6") and sources of payment (Medicare, Medicaid, worker's compensation, other government, commercial, HMO, self-pay, charity, other). (table 2). Multivariate logistic regression was done using the default method (enter mode) of entering covariates.

2.6.   RESULTS

Among 1,051,081 injury discharges, 2,709 (0.26%) had BCI; 13,087 (1.25%) had MVIIR; 9,811 (0.93%) had AVIIRS; 1,338 (0.13%) had TVIIRS and 178 (0.02%) had PVIIRS. Injuries to motor-vehicle occupant were the leading mechanism of injury for BCI (77%), followed by falls (6%) (see figure 1). Transportation-related injuries combined accounted for 87% of the attributed mechanisms for BCI. There were slightly fewer females with BCI (43.9%); however, there were more females with either type of valvular disorder (73.9% for MVIIR, 70.3% for AVIIRS, 69.4% for TVIIRS and 64.8% for PVIIRS) (see table 1). The overall rate (per 100,000 persons) for BCI, MVIIR, AVIIRS, TVIIRS, and PVIIRS was respectively 1.94, 9.37, 7.02, 0.96, 0.13. (see figures 2 and 3).

In the univariate analysis, BCI was significantly associated with MVIIR ($P < 0.001$), AVIIRS ($P < 0.001$), and TVIIRS ($P < 0.001$); and was not significantly associated with PVIIRS ($P > 0.05$). In the regression analysis, BCI was found to be a significant predictor for AVIIRS and for TVIIRS after adjustment for potential confounders (see table 2). BCI was not found to be a significant predictor for MVIIR and for PVIIRS after adjustment for potential confounders.

2.7.   DISCUSSION

BCI is a spectrum of injuries ranging from simple electrical conduction abnormalities to acute cardiac rupture.[55] Despite several studies, no consensus on standard diagnostic approach to evaluate BCI has been reached. Low incidence of BCI was found in a study where the cardiospecific enzymes were used yielding 19%.[23] Low incidence of BCI varying between 3 and 26% of patients with blunt chest trauma were also found in transthoracic echocardiography studies. [1,13,16,24,27,30,49] Incidences were higher when a transesophageal approach was used so that BCI was detected in 27-56% of the patients.[10,17,30,59] High incidences however,

were also found in ECG studies of patients with blunt chest trauma ranging from 29% to 56%. [7,23,24,27,49] Finally, using highly specific troponin I or T, incidences of BCI varied from 15% to 24%. [1,13,49]

Independent of age, race, sex, injury severity, and source of payment, we observed that BCI was associated with a 12-fold increased risk for TVIIRS. Acute severe elevation of right intraventricular pressure has been shown to result in injury of the tricuspid valvular apparatus.[44] Furthermore, the right ventricle is immediately behind the sternum, which make it more vulnerable to blunt trauma.[5] Rupture of the valve is more likely to occur if the injury occured during diastole when the right ventricular pressure is low,[34] particularly when the right ventricle is compressed between the sternum and the vertebrae column.[33] [9] The most frequently reported injury is chordal rupture, followed by rupture of the anterior papillary muscle and leaflet tear, primarily of the anterior leaflet.[44] The right ventricle has also been shown to be vulnerable to indirect injury by a sudden increase in intracardiac pressure from compression of the upper abdomen.[5]

We also found that independent of age, race, sex, injury severity, source of payment, and presence of ischemic heart disease, a person with BCI is 3.4 times more likely to have AVIIRS. The mechanism of "delayed" rupture has been shown to cause traumatic aortic regurgitation, explained by the presence of BCI.[43] Post-traumatic aortic valve regurgitation has been found to affect all ages and is often found with sternal or multiple rib fractures.[37] The valve damage is more likely to occur during systole or early diastole because of compressive forces that may arise following a deceleration injury. At this point in the cardiac pressure and volume cycle, the aortic valve is closed and the transvalvular gradient is maximal.[47]

41

Although we found that direct trauma to heart – namely BCI - was associated with MVIIR in the univariate analysis, we did not find that such trauma increases the risk of MVIIR in the multivariate regression analyses. The lack of association between BCI and MVIIR could be explained by the confounding by degenerative conditions such as myxomatous degeneration, which as we mentioned above, do not have ICD-9-CM. In some other studies, patients sustained traumatic mitral valve insufficiency have been shown to present with either entire papillary muscle avulsion from its ventricular attachment or with chordal and leaflet damage. [3,4] Those with papillary muscle avulsion presented with symptoms of acute mitral regurgitation with torrential regurge back into the left atrium.[3,11,14,18,20,22,39,52,61] Those patients who experienced chordal and leaflet damage presented with less severe clinical symptoms or were completely asymptomatic.[4,25,29,35,38,40,60]

There are limitations to consider when interpreting the results from this study. Despite adjusting for confounding factors, a strong temporal relationship between BCI and cardiac valvular disorders cannot be established through the current study design. Readers should bear in mind that this database contains discharge-level records, not patient-level records. This means that individual patients who are hospitalized several times in 1997 may be present in the dataset several times. There might be a higher probability of sustaining BCI in the presence of pre-existing valvular disease. Such probability may have been higher because cardiac tissues may have been weakened due to the effects of chronic dilation and hypertrophy such that compression of the cardiac chambers and increase of intracardiac pressure from injury forces were particular significant. On the other hand, pre-existing cardiac valvular disease might lead to a higher likelihood of the diagnosis of BCI being made, however, this database may provide only limited insight into this issue since acceptance of a specific diagnosis varies not only among hospitals

but also across physicians.[26,48,50] Medical chart review, although more expensive, may provide more detailed clinical information.

Another limitation is the fact that the three diagnostic codes reflecting AVIIRS, TVIIRS and PVIIRS may also include stenosis, which has not been shown to have a traumatic origin. This study was based on secondary data analysis, therefore under-reporting could occur.

Other problems related to administrative data include coding accuracy and limited ability to risk adjustment. [26,48,50]As mentioned earlier, diagnostic codes for MVIIR do not exclude myxomatous degeneration, which does not have an ICD-9-CM code. Myxomatous degeneration has been shown to be one of the leading causes for mitral valve insufficiency.[53] Long-standing mechanical stress was hypothesized to play a role in the wear and tear of the valve, resulting in valvular regurgitation.[51] Future research should answer the question whether the existing myxomatous degeneration may increase the risk of getting traumatic mitral valve insufficiency due to the long-term wear and tear of the valve.

We did not find that BCI increases the risk of PVIIRS. The lack of association between BCI and PVIIRS could be explained by a limited statistical power due to the sample sizes. There is no published research that has looked at traumatic pulmonary valvular insufficiency as the result of blunt chest trauma. PVIIRS is quite rare, and future research should focus on possible association between BCI and PVIIRS.

It is important to establish, quantify and better understand the relationship between blunt chest trauma and cardiac valvular disorders. Traumatic tricuspid valve insufficiency may necessitate early surgical treatment.[31] In general, valvular heart disease has been described as an important risk factor for congestive heart failure. Research shows that moderate-to-severe right heart failure eventually develops in patients with tricuspid valve injury, even though in

chordal rupture the estimated interval is 10-25 years.[15] Levy et al.[35] showed in the Framingham Heart Study that cardiac valvular disease confers more than twice the adjusted risk for development of congestive heart failure and a population-attributable risk of 7% to 8%. This issue becomes particularly important when it is noted that about 2 million people in the US suffer from congestive heart failure with 400,000 cases diagnosed each year.[18] It is the leading cause of hospitalization and a major cause of chronic disability among patients 65 or older.[21,22] Moreover, heart failure is the only major cardiovascular disease that is increasing in incidence and prevalence. [22]

Cardiac valve insufficiency has been well recognized as an important risk factor for congestive heart failure. With the findings that BCI is associated with an increased risk of specific valvular disorders, it is possible that trauma may play an important and heretofore largely unrecognized role in a portion of the burden of cardiovascular morbidity and mortality. Longitudinal studies with in-depth clinical information are needed to better quantify such burden. They may further our understanding of the relationship between BCI and cardiac valve insufficiency.

Table 2 Patient characteristics

Patient characteristics	BCI	MVIIR	AVIIRS	TVIIRS	PVIIRS
Age mean (SD)	54.6 (22.2)	71.7 (18.6)	82.1 (10.9)	78.1 (13.9)	74.7 (19.7)
Females (%)	1190 (43.9)	9672 (73.9)	6893 (70.3)	929 (69.4)	114 (64.8)
Nonwhite (%)	441 (16.3)	888 (6.8)	554 (5.6)	144 (10.8)	17 (9.7)
MAISS median	3	2	3	2	2

AVIIRS, aortic valve incompetence, insufficiency, regurgitation, stenosis; BCI, blunt cardiac injury; MAISS, maximum abbreviated injury severity score; MVIIR, mitral valve incompetence, insufficiency, regurgitation; PVIIRS, pulmonary valve incompetence, insufficiency, regurgitation, stenosis; SD, standard deviation; TVIIRS, tricuspid valve incompetence, insufficiency, regurgitation, stenosis
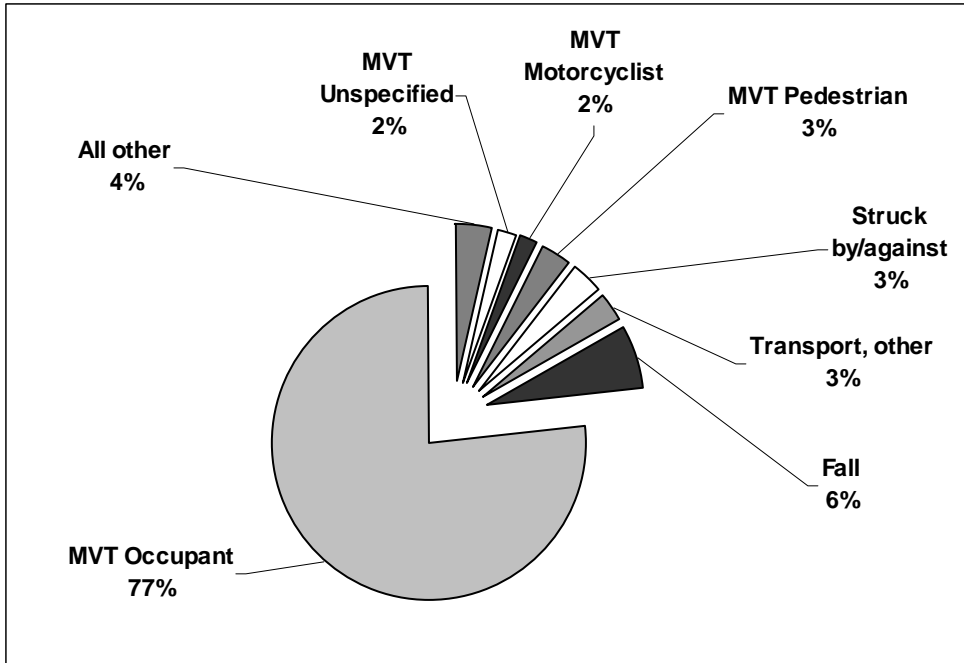
Figure 1 Mechanism of blunt cardiac injury

* Mechanisms that cause BCI in less than 1% cases were combined into "all other" category.

MVT, motor vehicle transportation
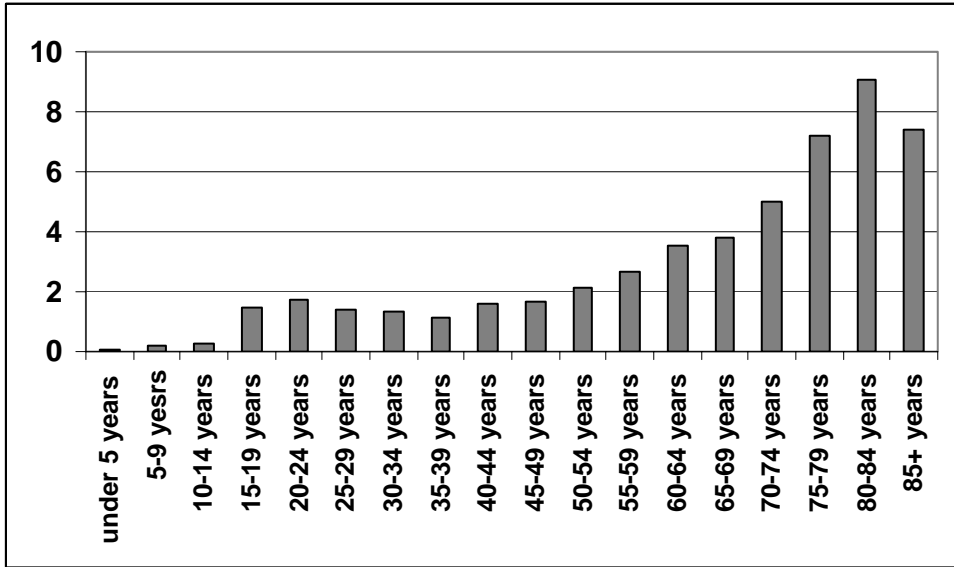
Figure 2 Hospitalized age-specific rates (per 100,000 persons) for blunt cardiac injury among different age groups
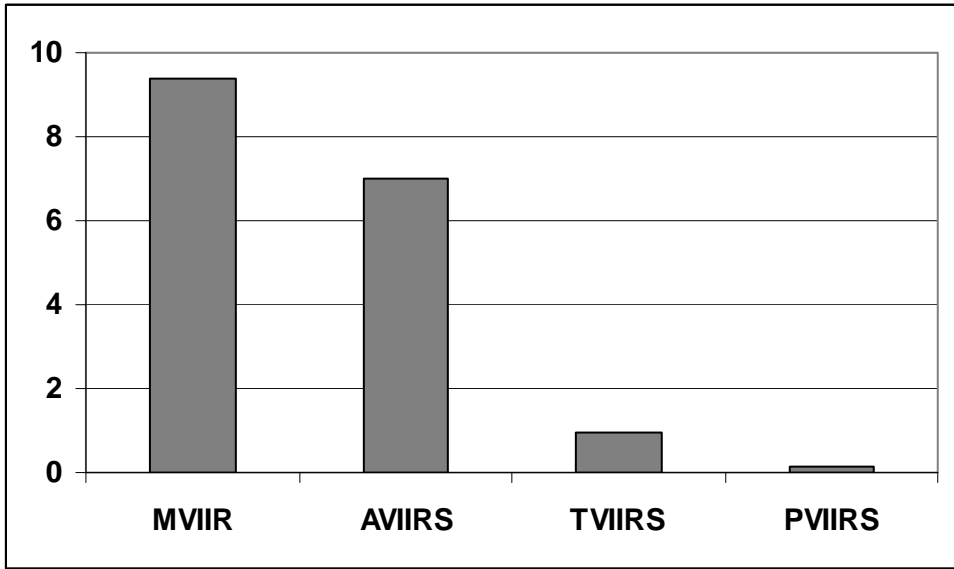
Figure 3 Hospitalized rate (per 100,000 persons) for MVIIR, AVIIRS, TVIIRS and PVIIRS

AVIIRS, aortic valve incompetence, insufficiency, regurgitation, stenosis; MVIIR, mitral valve incompetence, insufficiency, regurgitation**;** PVIIRS, pulmonary valve incompetence, insufficiency, regurgitation, stenosis**;** TVIIRS, tricuspid valve incompetence, insufficiency, regurgitation, stenosis

Table 3 Results of multivariate logistic regression analysis on AVIIRS and TVIIRS

Independent variable	AVIIRS OR (p-value)	TVIIRS OR (p-value)
BCI	3.41 (0.001)	11.54 (0.001)
Age (10 levels)	(< 0.001)	(< 0.001)
Race[#]	1.54 (0.017)	0.68 (0.024)
Sex[*]	1.08 (0.379)	1.07 (0.563)
MAISS (6 levels)	(0.418)	(< 0.001)
Sources of payment (9 levels)	(0.662)	(0.701)
Ischemic heart disease	1.38 (< 0.001)	N/A

AVIIRS, aortic valve incompetence, insufficiency, regurgitation, stenosis; BCI, blunt cardiac injury; MAISS, maximum abbreviated injury severity score; N/A, not applicable; TVIIRS, tricuspid valve incompetence, insufficiency, regurgitation, stenosis

[#] Referent group: white

[*] Referent group: males

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3. ARTICLE TWO: TRAUMA ASSOCIATED WITH ACUTE MYOCARDIAL INFARCTION IN A MULTI-STATE HOSPITALIZED POPULATION

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3.1. ABSTRACT

Introduction. Trauma has been suggested, in case series, as one of the nonatherosclerotic mechanisms leading to acute myocardial infarction (AMI), the leading cause of death in the US. AMI following non-penetrating injury has been shown to carry significant morbidity and mortality.

Objective. To determine whether hospitalized injuries in a large multi state population are associated with increased risk of AMI during the initial hospital stay.

Methods. Statewide injury hospital discharge data were collected from 19 states in 1997. Affected body regions of interest included thoracic, abdominal or pelvic, spine or back and blunt cardiac injury (BCI). The outcome of interest was AMI which was identified based on ICD-9-CM discharge diagnoses for the same visit. Unadjusted and adjusted multivariate logistic regression analyses were performed.

Results. Independent of confounding factors and coronary arteriography (CA) status, BCI was associated with 2.6-fold increased risk for AMI in persons 46 years or older. When the diagnosis of AMI was confirmed by CA, BCI was associated with 8-fold risk elevation among patients 46 years and older and a 31-fold elevation among patients 45 years and younger. Abdominal or pelvic trauma, irrespective of confounding factors and CA status, was associated with a 65% increase in the risk of AMI among patients 45 years and younger and 93% increase in the risk of among patients 46 years and older. When the diagnosis of AMI was confirmed by CA, abdominal or pelvic trauma was associated with 6-fold risk elevation among patients 46 years and older.

Conclusion. Direct trauma to the heart, as characterized by a diagnosis of blunt cardiac injury, was observed to carry the greatest risk for AMI. Abdominal or pelvic trauma also increased the risk for AMI. Longitudinal studies are warranted to better understand the relationship between trauma and AMI.

3.2.   KEY WORDS

Trauma, acute myocardial infarction

3.3.   ABBREVIATIONS

AMI: Acute myocardial infarction

BCI: Blunt cardiac injury

CA: Coronary arteriography

CI: Confidence interval

ISS: Injury Severity Score

MAISS: Maximum abbreviated injury severity score

OR: Odds ratio

3.4.   INTRODUCTION

Acute myocardial infarction (AMI) is the leading cause of death in the US, affecting about 900,000 persons annually.[1] Evidence from numerous case studies suggests that trauma is one of the nonatherosclerotic factors that associated with AMI particularly among young people (45 years old or younger).[2-12] Among older individuals (older than 46 years), coexisting atherosclerosis or preexisting atheromatous plaque may contribute to the appearance of AMI following a traumatic episode.[6]

According to case studies, AMI may occur immediately or shortly after trauma.[13-16] AMI following non-penetrating injury has been shown to carry significant morbidity and mortality.[17-21]

We examined whether certain types of hospitalized trauma (thoracic, abdominal/pelvic, spine/back or blunt cardiac injury (BCI), formerly known as myocardial contusion, are associated with increased risk of AMI. To test this hypothesis, we conducted a cross-sectional study of the association between trauma and AMI based on a database of all hospital discharges from 19 states during a one-year period.

3.5. METHODS

3.5.1. Subjects

A total of 19 states (Arizona, California, Florida, Massachusetts, Maryland, Maine, Michigan, Nebraska, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, South Carolina, Utah, Virginia, Vermont, Washington, and Wisconsin) provided hospital discharge data in 1997 based on ICD-9-CM classification (codes 800-959). From 17.8 million hospitalizations 1.05 million injury cases were found.

3.5.2. Exposure to injury

Injury cases were identified based on ICD-9-CM diagnosis codes representing injuries (800-959). The mechanism of injury and its associated intent were classified on the basis of the primary External Cause of Injury code, defined within ICD-9-CM. Thoracic trauma was identified based on the following codes: 807.0-807.4; 839.61-839.71; 848.3; 848.4; 860-862; 875; 879.0; 879.1; 901; 922.0; 922.1; and 942.x1-942.x2; abdominal and pelvic trauma was identified based on the following codes: 863-868; 878; 879.2-879.5; 902; 922.2; 922.4; 926.0; 942.x3; 947.3 and 947.4; spine and back traumas were identified based on the following codes:

805; 806; 839.0-839.5; 847; 876; 877; 926.11; 926.12; 942.x4 and 952. BCI was identified based on ICD-9-CM (861.01, "myocardial contusion").

3.5.3. AMI categorization

Acute myocardial infarction (AMI) was identified based on ICD-9-CM (410). Because BCI has many pathophysiologic similarities with an AMI, often confusing the diagnoses,[22,23] and since coronary arteriography (CA) has been shown to distinguish AMI from BCI,[24] we stratified individuals into those with AMI irrespective of CA status and those whose AMI was confirmed by CA. Patients undergoing CA were identified among those discharged with an AMI diagnosis based on procedure codes (8855, 8856 and 8857 respectively).

3.5.4. Statistical analysis

Unadjusted logistic regression analyses were used to examine the relationship between certain types of trauma (thoracic, abdominal/ pelvic, spine/back or BCI) and AMI. These analyses were performed separately for each outcome variable, i.e. AMI among persons 45 years and younger irrespective of CA status and confirmed by CA; and AMI among persons 46 years and older irrespective of CA status and confirmed by CA.

Six logistic regressions were constructed to model these outcomes against the following independent variables: 10 year age strata, gender (male versus female), presence of BCI (yes versus no), source of payment categories, thoracic trauma (yes versus no), abdominal or pelvic trauma (yes versus no), and spine or back trauma (yes versus no). Age adjustment was accomplished in two ways: (1) age was entered as a covariate in each regression model and (2) the data were divided in two datasets (45 years and younger and 46 years and older). The reason for this stratification was that ischemic heart disease is generally a disease of older people and this approach has been used by some other researchers.[25,26] Source of payment was

categorized as Medicare; Medicaid; worker's compensation; other government; commercial; HMO; self-pay; charity; other.

Other covariates considered in models were severity of injury, mechanism of injury, and drug and alcohol use. The ICDMAP-90 software (Center for Injury Research and Policy of the John Hopkins School of Public Health, Baltimore, MD, and Tri-Analytics, Inc., Bel Air, MD) was used to convert the diagnosis codes into Abbreviated Injury Scale (AIS).[27] Maximum abbreviated injury severity score (MAISS) was more often used in preference to other means of classifying injury severity due to its greater reproducibility.[28] It also provides researchers with a numerical method of ranking and comparing injuries by severity.[29] The Injury Severity Score (ISS)[30] reflects the more serious outcomes associated with multiple injuries. Since the two measures have been used in trauma centers to predict the probability of death, urgency of treatment and use of resources, both ISS and MAISS were used in the all regression models.[31] MAISS was entered as a categorical variable, the lowest being "0" and the highest being "6". ISS was entered as "Mild" (ISS 1-12), "Moderate" (ISS 13-19), "Severe" (ISS 20-75) or "Minor" (ISS 1-3), "Moderate" (ISS 4-7), "Serious" (ISS 8-15), "Severe to Critical" (ISS 16-75).[32]

Mechanism of injury was entered with either two categories ("Motor vehicle occupant and motor cycle occupant combined" versus "All other mechanisms combined") or three categories ("Motor vehicle occupant and motor cycle occupant combined", "Falls" and "All other mechanisms combined"). AMI has been recognized as a complication of cocaine abuse among young men and ethanol overdose may cause coronary vasospasm and death.[33,34,34-36] Cocaine use and alcohol use, both related to risk for injury[37-39], were entered as categorical variables. The default method (enter mode) of entering covariates (SPSS for Windows, version 12.0; SPSS, Chicago, Ill) was used for model construction.

3.6.   RESULTS

Among 1,051,081 injury discharges, 2,709 (0.26%) had BCI; 57,270 (5.45%) had thoracic trauma; 34,357 (3.27%) had abdominal or pelvic trauma; and 61,978 (5.90%) had spine or back trauma. Transportation-related injuries combined were the leading mechanism of injury associated with BCI (87%), thoracic trauma (33.2%) and abdominal or pelvic trauma (26.8%). Falls were the leading mechanism associated with spine or back trauma (43.2%).

Among all injury discharges, there were 32,616 (3.10%) that also included a discharge diagnosis of AMI. Among all injured individuals discharged with AMI, falls were the leading mechanism of injury (49.1%). Among persons 46 years or older discharged with AMI, falls (58%) remained the leading mechanism of trauma, followed by transportation-related injuries (22%). However, persons 45 years or younger discharged with AMI, the leading mechanism of injury was transportation-related (31%) followed by poisoning (20%) and falls (13%).

Patient characteristics of injury discharges with AMI and without AMI are presented in Table 1. There were fewer males (45.9%) and more whites (76.9%) among all injury discharges with AMI compared to all injury discharges without AMI (more males (49.0%) and less whites (67.8%).

In unadjusted logistic regression analysis, BCI and abdominal or pelvic trauma were significantly associated with increased risk of AMI in both 45 years or younger and 46 years or older age groups and in person with and without CA. The only exception was that abdominal or pelvic trauma was significantly associated with decreased risk of AMI documented by CA among persons 45 years or younger. Thoracic trauma was significantly associated with moderate increased risk of AMI in both 45 years or younger and 46 years or older age groups. Spine or back trauma was not found to be a significant predictor for AMI in unadjusted analyses (Tables 2 and 3).

Independent of confounding factors and coronary CA status, direct trauma to the heart was associated with 2.6-fold (OR 2.64 95% CI 1.49 – 4.66) increased risk for AMI in persons 46 years or older. When the diagnosis of AMI was confirmed by CA, BCI was associated with 8-fold (OR 8.38 95% CI 2.29 – 30.71) risk elevation among patients 46 years and older and a 31-fold (OR 31.44 95% CI 5.34 – 185.04) elevation among patients 45 years and younger. Abdominal or pelvic trauma, irrespective of confounding factors and CA status, was associated with a 65% (OR 1.65 95% CI 1.26 – 2.16) increase in the risk of AMI among patients 45 years and younger and 93% (OR 1.93 95% CI 1.42 – 2.62) increase in the risk of among patients 46 years and older. When the diagnosis of AMI was confirmed by CA, abdominal or pelvic trauma was associated with 6-fold (OR 6.33 95% CI 4.00 – 9.99) risk elevation among patients 46 years and older. Thoracic trauma, irrespective of confounding factors and CA status, was associated with 24% (OR 1.24 95% CI 1.03 – 1.50) increase in the risk of AMI among patients 46 years and older. Spine or back trauma was not found to be a significant predictor for AMI in adjusted analyses (Tables 2 and 3).

3.7.   DISCUSSION

A substantial external impact is likely needed to damage the intimae of nonatherosclerotic coronary arteries. Motor vehicle crashes have been shown to produce such significant and sudden deceleration.[40] In our study, transportation-related trauma was the leading mechanism of injury among persons 45 years old or younger and this finding correlates well with the evidence from case studies that looked at AMI following motor vehicle crashes. [41-44] Although compression of the anterior chest wall during traumatic impact has been shown to cause damage to the intimae of the coronary arteries[45], we, however, found that thoracic trauma was related to only moderately increased risk for AMI after adjusting for other variables.

BCI was strongly associated with AMI in our study. Independent of confounding factors and CA status, direct trauma to the heart was associated with a 2.6-fold increased risk for AMI in persons 46 years or older. BCI was found to be even a stronger predictor if CA was performed and the diagnosis of AMI was confirmed (8-fold risk elevation among patients 46 years and older and a 31-fold elevation among patients 45 years and younger). Diagnostic catheters for angiography have been shown to cause iatrogenic cardiac trauma.[46] On the other hand, since coronary arteries, particularly the left descending coronary artery, lie superficially on the muscle wall, direct trauma to the coronary arteries with the resultant acute formation of coronary thrombosis has been considered as one of the probable mechanisms of trauma-related AMI.[47] A shear force applied directly to the coronary artery may cause intimal tearing which may further result in platelet aggregation and intracoronary thrombosis.[48] Finally, existent atherosclerotic plaque might also predispose the coronary artery to traumatic disruption.[45] Misclassification of BCI for AMI is unlikely to have occurred in our study since we have shown that there was an increased risk of AMI among individuals with CA while other mechanisms were not associated with increased risk in the CA group. In addition, thoracic trauma, a well-known risk factor for BCI,[49,50] represented a consistently higher proportion of all injuries among individuals diagnosed with AMI compared to individuals without AMI which makes over diagnosis of BCI among AMI unlikely.

Abdominal or pelvic trauma, irrespective of confounding factors and CA status, was associated with a 65% increase in the risk of AMI among patients 45 years and younger and a 93% increase among patients 46 years and older. There was a 6-fold increase risk of AMI among patients 46 years and older where AMI could be distinguished from BCI by performing CA. Increase of intravascular hydrostatic pressure occurs with sudden compression or crushing of the

abdomen.[47,51] The mechanism of such trauma was described by Beck.[51] In addition, cases of combined abdominal trauma and cardiac injury have been reported.[52-55] Finally, a sudden compression of the abdomen leads to accelerated boundary layer separation on the curved surface of the vessel and may also result in increase in the shear stress which, in turn, may damage the endothelium. [56] Sudden elevation of intra-aortic pressure caused by sudden external impact to the abdominal area may possibly result in rupture of the coronary vessel particularly if the aortic valve was closed during the traumatic impact (during systole). In a study by Ochsner et al.[40] 83% of aortic ruptures occurred in patients with an anterior-posterior pelvic fracture pattern, and an incidence of aortic rupture was more than 9 times greater in these patients than the incidence of aortic rupture in the overall blunt trauma population (7.5% vs. 0.8; $p<0.001$). In our study, risk for AMI related abdominal or pelvic injury may have been particularly high among people 46 years and older because abdominal muscles or pelvic ligaments may have been weakened due to aging such that compression of the aorta, resulting blood deceleration and increase of intravascular hydrostatic pressure were particularly significant.

There are several limitations pertaining to our study. An accurate temporal relationship between trauma and AMI could not be established due to the cross-sectional nature of the study design. Furthermore, under-reporting of exposures and outcomes could have occurred since both were captured through ICD coding and this could have potentially biased our results.

Patients with abdominal, pelvic or blunt cardiac injury (BCI) might benefit from certain screening procedures for AMI such as ECG or cardiac enzyme analysis. Such procedures may also help to prevent late cardiac complications of AMI such as ventricular fibrillation. Therefore, it is important to recognize that trauma may be a risk factor for AMI.

This study provides the first population-based epidemiological evidence in support of this possibility. Patients with AMI following trauma may have significant left ventricular dysfunction with poor prognosis even after other traumatic injuries have healed.[45] While abdominal or pelvic trauma increased the risk for AMI, a direct trauma to the heart -- namely BCI -- created the greatest risk for AMI. Longitudinal studies are warranted to better understand the relationship between trauma and AMI.

Table 4 Patient characteristics

	All injury discharges with AMI	All injury discharges without AMI
Age (mean)	67.84	51.7
Males (%)	14,984 (45.9%)	499,301 (49.0%)
Whites (%)	25,089 (76.9%)	690,137 (67.8%)
MAISS (median)	2	2
Thoracic trauma (%)	2,116 (6.5%)	55,154 (5.4%)
Abdominal or pelvic trauma (%)	1,534 (4.7%)	32,823 (3.2%)
Spine or back trauma (%)	1,917 (5.9%)	60,061 (5.9%)
BCI	201 (0.6%)	2,508 (0.2%)
Alcohol use	2,605 (8.0%)	61,401 (6.0%)
Cocaine use	192 (0.6%)	6,049 (0.6%)

AMI: Acute myocardial infarction

BCI: Blunt cardiac injury

MAISS: Maximum abbreviate injury severity score

Table 5 Odds ratios obtained from unadjusted and adjusted logistic regression analysis on discharges with all AMI and AMI confirmed by CA among patients 45 years and younger

	All AMI		AMI confirmed by CA	
	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Thoracic trauma	1.23 (1.10-1.38)	0.78 (0.55-1.11)	1.11 (0.45-2.72)	1.19 (0.36-3.95)
Abdominal/pelvic trauma	1.96 (1.81-2.16)	1.65 (1.26-2.16)	0.57 (1.18-1.81)	0.88 (0.21-3.76)
Spine or back trauma	0.89 (0.78-1.00)	0.89 (0.60-1.34)	0.39 (0.10-1.57)	0.37 (0.05-2.68)
BCI	4.14 (3.09-5.54)	1.38 (0.59-3.25)	10.09 (2.48-40.96)	31.44 (5.34-185.04)

AMI: Acute myocardial infarction

CA: Coronary arteriography

CI: Confidence interval

BCI: Blunt cardiac injury

OR: Odds ratio

* Adjusted for age, gender, race, the injury severity score (ISS), maximum abbreviated injury severity score (MAISS), mechanism of injury, source of payment, cocaine and alcohol use.

Table 6 Odds ratios obtained from unadjusted and adjusted logistic regression analysis on discharges with all AMI and AMI confirmed by CA among patients 46 years and older

	All AMI		AMI confirmed by CA	
	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Thoracic trauma	1.09 (1.05-1.15)	1.24 (1.03-1.50)	1.09 (0.86-1.39)	1.06 (0.62-1.83)
Abdominal/pelvic trauma	2.22 (2.08-2.38)	1.93 (1.42-2.62)	5.78 (4.69-7.12)	6.33 (4.00-9.99)
Spine or back trauma	0.93 (0.88-0.98)	1.21 (0.96-1.53)	0.79 (0.61-1.04)	0.74 (0.36-1.52)
BCI	2.02 (1.71-2.38)	2.64 (1.49-4.66)	2.55 (1.27-5.11)	8.38 (2.29-30.71)

AMI: Acute myocardial infarction

CA: Coronary arteriography

CI: Confidence interval

BCI: Blunt cardiac injury

OR: Odds ratio

* Adjusted for age, gender, race, the injury severity score (ISS), maximum abbreviated injury severity score (MAISS), mechanism of injury, source of payment, cocaine and alcohol use.

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4. ARTICLE THREE: TRAUMA ASSCOCIATED WITH CARDIAC ARRHYTHMIAS: RESULTS FROM A LARGE MATCHED CASE-CONTROL STUDY

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4.1. ABSTRACT

Introduction. Various cardiac arrhythmias such as supraventricular and ventricular premature beats, supraventricular and ventricular paroxysmal tachycardia, atrial and ventricular fibrillation and atrial flutter have been reported as complications of blunt cardiac and thoracic trauma. The objective of this research was to determine whether thoracic or blunt cardiac injury is associated with cardiac arrhythmias in a large multi-state hospitalized population.

Methods. Cases and matched (by age) controls were identified based on hospital discharge information that was collected from 986 acute general hospitals across 33 states in 2001. Both the exposure (thoracic trauma and blunt cardiac injury) and the outcome (cardiac arrhythmias) were identified based on ICD-9-CM discharge diagnoses. Unadjusted and conditional adjusted (for gender, race, length of stay and primary source of payment) multivariate logistic regression analyses were performed.

Results. After adjusting for potential confounders, patients 45 years and younger diagnosed with blunt cardiac injury had 13-fold [95% confidence interval (CI), 2.98; 53.91] increase in the risk of cardiac arrhythmia.

Conclusion. Blunt cardiac injury was found to be a significant risk factor for cardiac arrhythmia. Longitudinal studies are needed to better establish the association between thoracic trauma and cardiac arrhythmias.

4.2. KEY WORDS

4.3.   INTRODUCTION

Cardiac arrhythmias have been frequently reported in case reports as a complication of trauma (Bertinchant et al., 2000; Sakka et al., 2000; Brokhes, 1970; Singer et al., 1998; Ellis and Hutchinson, 2000; McLean et al., 1991; van Wijngaarden et al., 1997; Fabian et al., 1991; Berk, 1987; Liedtke et al., 1974; Attenhofer et al., 1992; Leor et al., 1990; Sokolov et al., 1979; Ganelina et al., 1974; Bodin et al., 1988; Inoue et al., 2004; Hoiting and Harrahill, 2000). Thoracic trauma and blunt cardiac injury have been shown to produce various types of arrhythmias such as ventricular and supraventricular extrasystoles (Potkin et al., 1982; Wisner et al., 1990; Mehta et al., 1990; Guy et al., 2000), atrial fibrillation and flutter (Singer et al., 1998; Ellis and Hutchinson, 2000; Fulda et al., 1997; McLean et al., 1991; Fabian et al., 1991; Attenhofer et al., 1992; Hosaka et al., 2004), supraventricular and ventricular paroxysmal tachycardia (Vogler and Seaberg, 2001; McLean et al., 1991; Fabian et al., 1991; Mehta et al., 1990; Leor et al., 1990; Sokolov et al., 1979; Ganelina et al., 1974; Bodin et al., 1988) and ventricular fibrillation (Inoue et al., 2004; Hosaka et al., 2004; Niedeggen and Wirtz, 2002). Traumatic cardiac arrhythmias have been observed after being hit by a brick (Singer et al., 1998), by a steering column(Vogler and Seaberg, 2001) and by a soccer ball(Leor et al., 1990). Fabian et al.(Fabian et al., 1991) described 92 patients who experienced various cardiac arrhytmias after anterior chest impact (i.e. sternal or rib fractures) while Leor et al.(Leor et al., 1990) (Leor et al., 1990) observed multiple ventricular premature contractions in patient with blunt trauma to the left precordium. In some studies, patients who developed cardiac arrhythmia had no history of cardiovascular diseases in the past(Bertinchant et al., 2000; Bodin et al., 1988). Traumatic cardiac arrhythmias usually developed within the first several hours (Mayfield and Hurley, 1984;

Harley et al., 1984) or within 24-48 hours after injury (Illig et al., 1991; Wisner et al., 1990; Silverman et al., 1990; Norton et al., 1990), however, patients with trauma may experience life-threatening arrhythmias even after several days following episode of injury (Sakka et al., 2000).

Our previous study has shown that trauma may be associated with such serious cardiac event as acute myocardial infarction even after controlling for potential confounding factors (Ismailov et al.,). Although potentially treatable, cardiac complications of thoracic or cardiac trauma such as heart failure or cardiac arrhythmias are difficult to predict (Biffl et al., 1994; Curfman, 1998). The objective of this research, therefore, was to determine whether thoracic and blunt cardiac injuries are significantly associated with certain cardiac arrhythmias. A matched case-control study of the association between thoracic and blunt cardiac injuries and cardiac arrhythmias was conducted based on a database of all hospital discharges from 33 states.

4.4.   METHODS

The Agency for Healthcare Research and Quality (AHRQ) developed the 2001 Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) (http://www.hcup-us.ahrq.gov/db/nation/nis/Overview_of_NIS_2001_25Jul03.pdf). The 2001 NIS file has 7.45 million uniform hospital discharge abstracts for all inpatient stays. Such discharge information was collected from 986 acute care general hospitals across 33 states (Arizona, California, Colorado, Connecticut, Florida, Georgia, Hawaii, Illinois, Iowa, Kansas, Kentucky, Maryland, Massachusetts, Maine, Minnesota, Missouri, Montana, Nebraska, North Carolina, New Jersey, New York, Oregon, Pennsylvania, Richmond, South Caroline, Tennessee, Texas, Utah, Virginia, Vermont, Washington, Wisconsin, West Virginia). The NIS contains patient-level characteristics, types and sources of admissions, ICD-9-CM diagnosis codes, procedure codes, diagnosis related groups, total charges, primary and secondary sources of payment, insurance

coverage, discharge status, length of stay and procedure days from admission (Boxer et al., 2003; Elixhauser et al., 2003).

Thoracic trauma was identified based on ICD-9-CM diagnostic codes: 807.0-807.4; 839.61-839.71; 848.3; 848.4; 860-862; 875; 879.0; 879.1; 901; 927.0; 922.1 and 942.x1-942.x2. Body part groupings were based on an early version of the Barell Matrix developed by Barell et al. (Barell et al., 2002). Blunt cardiac injury was identified based on ICD-9-CM diagnostic code (861.01). Cardiac arrhythmias were identified based on ICD-9-CM (420) (Table 1).

The rates for each of the cardiac arrhythmias of interest were initially examined. Patient-level characteristics included age, race (whites versus non-whites) and gender (male versus female). Length of stay was categorized as a categorical variable (3 days or less versus more than 3 days). Primary source of payment included Medicare, Medicaid, private including HMO, self-pay, no charge and other.

There were totally 672,043 cases with arrhythmia of interest (table 1) included in this study. All arrhythmias of interest were combined into one outcome. The controls were matched for age ($\pm$ 1.5 years) in the ratio 1:1 by random selection subset within each age group. Random selection was also conducted by creating a random variable that was used to sort controls. Subsets of data with randomly selected controls were subsequently merged to subsets of data with cases. Characteristics of cases and controls are given in table 2. All controls were free of reported arrhythmia based on ICD-9-CM codes.

Paired (i.e. cases versus controls) analysis on exposure of interest based on 3 year age group was conducted (tables 3 and 4). It is the requirement of the AHRQ to report only those subsets of analysis where "the number of observations (i.e. individual discharge records) in any given cell of tabulated data is less than or equal to 10."(Boxer et al., 2003) Therefore, those cells

where the number of observations were less or equal to 10 were collapsed (tables 3 and 4) (Elixhauser et al., 2003)

Unadjusted logistic regression analyses were used to examine the relationship between thoracic trauma, blunt cardiac injury and cardiac arrhythmia (tables 5 and 6). The multivariate extension for McNemar Test for matched case-control study (the Conditional logistic regression) was used to assess the multivariate relationship between thoracic trauma, blunt cardiac injury, multiple patient characteristics and the probability of cardiac arrhythmia. To test interaction a product term was calculated by multiplying dichotomized exposure of interest (i.e. thoracic or blunt cardiac injury) with variable reflecting each 10 year age group strata. The interaction term was included in a model along with all available potentially confounding covariates: gender, race, length of stay and source of payment. Models with and without interaction terms were analyzed revealing a thoracic injury-age (51 – 60) interaction and a thoracic injury-age (61 – 70) interaction product terms that were statistically significant. Therefore, we identified 2 cut-points for the analysis on thoracic injury and cardiac arrhythmia. Since there was no a blunt cardiac injury-age interaction, we chose 45 years cut-off point as in our previous study.(Ismailov et al.,) This approach has been also used by other researchers. (Romelsjo et al., 2003; Morillas et al., 2002) When appropriate, odds ratios (ORs) and 95% confidence intervals (CIs) were given. Calculations were performed using SPSS for Windows (version 12.0; SPSS, Chicago, Ill.)

4.5. RESULTS

Among 672,042 cases of arrhythmia, 988 (0.15%) had thoracic trauma and 126 (0.02%) had blunt cardiac injury. Among 672,042 controls, 1193 (0.18%) had thoracic trauma and 90 (0.01%) had blunt cardiac injury. Social and demographic characteristics of cases and controls are

presented in table 4. There were fewer females (50.9 versus 59.3) and more whites diagnosed with cardiac arrhythmia (64.9 versus 59.8) compared to controls.

In unadjusted logistic regression analyses, thoracic trauma was significantly associated with moderately decrease in the risk for cardiac arrhythmia among patients 71 years and older while blunt cardiac injury was significantly associated with increased risk for cardiac arrhythmia among patients 45 years and younger (tables 5 and 6). In the multivariate conditional logistic regression analyses, blunt cardiac injury was found to be a significant risk factor for cardiac arrhythmia among patients 45 years and younger (table 5). After adjusting for potential confounders, discharge for thoracic trauma was found to have moderately decreased risk for cardiac arrhythmia among people 71 years and older (table 6).

4.6. DISCUSSION

This paper represents the first attempt to look at the association between thoracic and cardiac trauma and cardiac arrhythmias at a large population based level. Population-based studies are important in that they reduce the potential for selection bias and confounding both of which may limit the interpretation of case reports. In addition, population based studies which include control groups provide quantitative estimates of association as well as better estimates of public health impact.

We found that patients 45 years and younger diagnosed with blunt cardiac injury had 13-fold increase in the risk of cardiac arrhythmia. Several mechanisms have been hypothesized to explain cardiac arrhythmias resulting from trauma including abnormal perfusion patterns, vagal sympathetic reflex and abberant conduction by damaged myocardial cells (Darok et al., 2001). Local hypoxia and ischemia caused by increased intravascular rouleaux formation due to trauma (Ismailov, 2005) may also contribute to the mechanism of traumatic cardiac arrhythmias. The

mechanism of traumatic cardiac arrhythmias was studied in animals. Schlomka conducted a series of experiments where he traumatized the heart by direct blows. Both ventricular tachycardia and fibrillation were observed (Parmley et al., 1958). Link et al.(Link et al., 1998) conducted a series of low energy impacts to the chest wall in a swine model. It has been demonstrated that the risk and type of arrhythmia depend on when the impact occurred during the cardiac electric cycle (Link et al., 1998; Cooper and Taylor, 1989). In addition, the risk of cardiac arrhythmia was found to be directly proportional to both the force and speed of the impact and inversely proportional to the size of the contact area. (Link et al., 1998). Evidence that cardiac arrhythmias may result from relatively 'mild' sport traumas perhaps suggesting that the strength of the impact is less important has been also introduced by various researchers who noticed that various types of arrhythmias may appear from usually innocent-appearing chest blows in various sport activities (Wallen et al., 1995). On the other hand using the swine model it was shown that even low energy impact can have immediate and significant effect of applied during a short and vulnerable time interval (i.e. upstroke of the T wave) resulting in ventricular fibrillation (Link et al., 1998).

Atrial fibrillation, one of the most common cardiac arrhythmias encountered in clinical practice (Prystowsky et al., 1996) was found to be the most common form of arrhythmia that presents after chest injury (Healey et al., 1990; Olsovsky et al., 1997; Singer et al., 1998; Ellis and Hutchinson, 2000; Fulda et al., 1997; McLean et al., 1991; van Wijngaarden et al., 1997; Norton et al., 1990; Cachecho et al., 1992; Fabian et al., 1991; Attenhofer et al., 1992; Hosaka et al., 2004). In the study conducted by Seguin et al.(Seguin et al., 2004), independent of confounding factors, blunt thoracic trauma was associated with 17-fold increased risk for atrial fibrillation. The relatively short observation of patients for the presence of some confounding

factors such as the presence or absence of shock as well as the relatively low incidence of atrial fibrillation were the main limitations of this study. Another limitation of this study was the lack of assessment for blunt cardiac injury among patients with blunt thoracic injury which may explain the disagreement in results between this and our study.

Although chronic cardiovascular conditions, such as ischemic heart disease or rheumatic diseases are major cause of atrial fibrillation, in about 10% of people with this type of arrhythmia, the "true" cause is unknown (Fuster et al., 2001; Stollberger et al., 2004). Blunt cardiac injury was found to be one of the causes of atrial fibrillation but this type of injury is difficult to diagnose (van Wijngaarden et al., 1997; Norton et al., 1990; Cachecho et al., 1992). In a previous study, we have found that blunt cardiac injury is much less frequent when identified through ICD-9-CM and when compared to thoracic injury (57,270 versus 2,709 respectively) (Ismailov et al.,). The NIS data has even fewer cases of blunt cardiac injury which might be explained by more uniform approach to diagnose this type of trauma injury after the consensus on diagnostic criteria has been published in 1998. (Pasquale et al.,)In addition, relatively 'mild' mechanical impact to the chest can result in serious cardiac arrhythmia even without significant blunt cardiac injury (Nesbitt et al., 2001; Link et al., 1999). On the other hand, cardiac injury may be produced by external traumatic agent without symptoms of significant chest trauma. (Juan et al., 2002) This probably can explain the lack of association between chest trauma and cardiac injury in our study.

Both supraventricular and ventricular paroxysmal tachycardia have been reported following thoracic and cardiac trauma (Vogler and Seaberg, 2001; McLean et al., 1991; Fabian et al., 1991; Mehta et al., 1990; Leor et al., 1990; Sokolov et al., 1979; Ganelina et al., 1974; Bodin et al., 1988). Most traumatic cardiac arrhythmias and ECG changes are transitory

conditions that are usually represented as ST-T changes or extrasystoles (Potkin et al., 1982; Wisner et al., 1990; Attenhofer et al., 1992; Mehta et al., 1990; Bodin et al., 1988; Guy et al., 2000; Hoiting and Harrahill, 2000). Some traumatic cardiac arrhythmias, however, such as ventricular fibrillation may lead to immediate death (Inoue et al., 2004; Hosaka et al., 2004; Niedeggen and Wirtz, 2002). This phenomenon is poorly understood and in some cases is described as commotion cordis, a life-threatening even occurring mostly in young sportsmen (Maron et al., 2002; Maron et al., 1999; Maron et al., 1997; Maron et al., 1995). Although commotion cordis is a relatively rare event, its prevalence is likely underestimated (Link et al., 1998; Link et al., 1999; Maron et al., 1999).

There are several limitations related to this study. Due to the nature of the data (i.e. administrative), temporal trends between trauma and cardiac arrhythmias could not be established. There might be a higher probability of sustaining cardiac arrhythmia in the presence of pre-existing cardiac disease, however, this database can not provide any insight into this issue since administrative data may not provide accurate insight into timing of events. Certain other problems such as coding accuracy and variation as well as a limited insights into temporal relationship between events have been related to administrative data (Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999). In addition, such data may not provide full clinical information (Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999). Medical chart review, although more expensive, may provide more detailed information on both the exposure and the disease (Miller et al., 2003), while longitudinal studies would provide in-depth insight into timing of events. Finally, while we have gained power by combining all arrhythmias into one group, but also lost the precision of the individual types of arrhythmia.

It is important to establish the nature and degree of association between of certain types of trauma, such as cardiac and thoracic, and arrhythmias. Ventricular paroxysmal tachycardia can degenerate spontaneously into ventricular fibrillation or may result in congestive heart failure (Stewart et al., 1986; Anonymous2000). However, it may be even more important to establish a between trauma and supraventricular paroxysmal tachycardia since such patients may be completely asymptomatic. Nevertheless, depending on coexisting cardiac diseases, such arrhythmia can cause pulmonary edema or myocardial ischemia (Ganz and Friedman, 1995; Xie et al., 1998). Patients with blunt cardiac injury, therefore, might benefit from certain screening procedures for cardiac arrhythmias such as ECG although normal ECG on admission and during 24 hours in ICU does not exclude fatal cardiac arrhythmias after discharge (Sakka et al., 2000). Results of this study, however, do not lend themselves to aggressive screening for cardiac arrhythmias, rather, they suggest more research in this particular direction. Future research should also focus on possible association between other types of trauma such as back or abdominal trauma and cardiac arrhythmias.

Table 7 Cardiac arrhythmias of interest

Cardiac arrhythmias	ICD-9-CM code
Premature beats, supraventricular	427.61
Paroxysmal supraventricular (includes tachycardiaatrial, atrioventricular, junctional, nodal)	427.0
Atrial flutter	427.32
Atrial fibrillation	427.31
Premature beats, ventricular	427.69
Paroxysmal ventricular tachycardia	427.1
Ventricular fibrillation	427.41

Table 8 Paired analysis on thoracic injury among cases and controls

Age groups	++	+ -	- +	- -
0- 33 years	32	21	11	12794
34 - 42 years	30	17	13	14710
43 - 48 years	38	18	20	23982
49 - 54 years	70	32	38	39190
55 - 57 years	47	19	28	26705
58 - 60 years	55	16	39	38573
61- 63 years	55	20	35	46947
64 - 66 years	55	21	34	50339
67 - 69 years	89	40	49	78719
70 - 72 years	119	51	68	88271
73 - 75 years	158	77	81	128094
76 - 78 years	210	85	125	157432
79 - 81 years	233	103	130	146157
82 - 84 years	290	131	159	158020
85 - 87 years	233	120	113	123569
88 - 90 years	213	96	117	103591
91 - 93 years	154	68	86	63122
94 - 96 years	65	32	33	27969
97 – 100 years	35	21	14	13721
Total	**2181**	**988**	**1193**	**1341905**

Table 9 Paired analysis on blunt cardiac injury among cases and controls

Age group	+ +	+ -	- +	- -
0 – 57 years	59	48	11	117539
58 – 69 years	40	24	16	214792
70 – 75 years	26	13	13	216616
76 – 81 years	45	17	28	303987
82 – 90 years	29	15	14	282083
91 – 100 years	46	24	22	490936
Total	216	126	90	1343870

Table 10 Social and demographic characteristics of cases and controls

Characteristics	Cases (672,043)	Controls (672,043)
Females (%)	342,565 (50.9)	398,295 (59.3)
Whites (%)	436,232 (64.9)	401,572 (59.8)
Length of stay (median)	5	4
Medicare	522,193 (77.7)	515,303 (76.7)
Medicaid	21,100 (3.1)	25,881 (3.9)
HMO	109,719 (16.3)	108,155 (16.1)
Self-pay	8,842 (1.3)	10,299 (1.5)
No-charge	641 (0.1)	686 (0.1)
Thoracic trauma	988 (0.1)	1,193 (0.2)
Blunt cardiac injury	126 (0.02)	90 (0.01)

Table 11 Results of the conditional multivariate logistic regression analysis on blunt cardiac injury and cardiac arrhythmias

	45 years and younger			46 years and older		
	OR	P-value	CI, 95%	OR	P-value	CI, 95%
Blunt cardiac injury, unadjusted	15.66	0.001	(3.75; 65.48)	1.08	0.607	(0.81; 1.44)
Blunt cardiac injury, adjusted	12.67	0.001	(2.98; 53.91)	1.06	0.690	(0.79; 1.42)

Table 12 Results of the conditional multivariate logistic regression analysis on thoracic injury and cardiac arrhythmias

	50 years and younger			51 to 70 years			71 years and older		
	OR	P-value	CI, 95%	OR	P-value	CI, 95%	OR	P-value	CI, 95%
Thoracic injury, unadjusted	0.939	0.760	(0.64; 1.41)	0.90	0.242	(0.76; 1.07)	0.80	0.001	(0.72; 0.88)
Thoracic injury, adjusted	1.35	0.114	(0.93; 1.97)	1.11	0.262	(0.93; 1.34)	0.72	0.001	(0.65; 0.80)

4.7.   LITERATURE CITED

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5.   DISCUSSION

5.1.   SUMMARY OF THE RESULTS

We evaluated the association between various types of trauma such as thoracic, abdominal, pelvic and cardiac traumas and certain cardiovascular disorders namely cardiac valve insufficiency, acute myocardial infarction and cardiac arrhythmias.

In specific aim 1, we investigated the association between direct trauma to heart (blunt cardiac injury) and cardiac valve insufficiency. We found that blunt cardiac injury is associated with 3 fold increased risk of aortic valve disorder and 12 fold risk of tricuspid valve disorder during the initial visit. Although numerous clinical case reports looked at the association between trauma and cardiac valve disorders, we conducted, for the first time, a population-based study that has looked at the association between these two conditions of interest.

In specific aim 2, we investigated the association between various types of trauma such as blunt cardiac injury, thoracic, abdominal, pelvic and back traumas and acute myocardial infarction. Independent of confounding factors and coronary arteriography status, direct trauma to the heart was associated with a 3-fold increased risk for acute myocardial infarction in persons 46 years or older. When the diagnosis of acute myocardial infarction was confirmed by coronary arteriography, BCI was associated with a 5-fold risk elevation among patients 46 years and older and a 44-fold elevation among patients 45 years and younger. Abdominal or pelvic trauma, irrespective of confounding factors and coronary arteriography status, was associated with a 70% increase in the risk of acute myocardial infarction among patients 45 years and younger and a 3-fold increase among patients 46 years and older.

This study was the first population based attempt to look at the association between various injuries and acute myocardial infarction at the population based level. Previously, several case reports found that direct trauma to heart may result in acute myocardial infarction, however, because of their design, the interpretation of the results was limited due to confounding and bias.

In specific aim 3, we investigated the association between thoracic trauma and cardiac arrhythmias. We found that blunt cardiac injury is a significant risk factor for cardiac arrhythmias.

5.2.   STRENGTHS AND LIMITATIONS OF OUR STUDIES

The strength of our studies was that they were very large and population based; identifying trauma as a risk factor for a chronic condition that represents a major public health issue. In case series, although various types of trauma have been suggested as a risk factor for cardiovascular disorders, evidence linking these two areas have lacked population based studies. Case reports provided some evidence suggesting an association between trauma and cardiovascular disorders however, population-based studies are important in that they reduce the potential for selection bias and confounding, both of which may limit the interpretation of case reports. In addition, population based studies which include control groups provide quantitative estimates of association.

Study outcomes in the case of cardiac valve insufficiency were identified based on the ICD-9-CM codes that excluded conditions which have not been shown to be associated with injury. For instance, aortic valve insufficiency was identified based on ICD-9-CM (424.1) that excludes hypertrophic subaortic stenosis (425.1), and aortic valve insufficiency caused by rheumatism (395.0-395.9). Further, in regression analysis, certain adjustments were made to control for other possible causes of traumatic cardiac events. In the case of traumatic cardiac

valve insufficiency, for instance, we controlled for ischemic heart disease, degenerative conditions (by controlling for age) and for other possible confounders.

Due to our study designs, a strong temporal relationship between trauma and cardiovascular diseases could not be established. Administrative data does not allow researchers to differentiate whether patients developed the condition while staying in the hospital or before the admission.(Miller et al., 2003; Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999)

In general, hospital discharge data are useful only when certain limitations are taken into account. Because coding practices may vary across hospitals, codes are subject to certain degree of variation and accuracy.(Miller et al., 2003; Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999) Both cases of injuries and cardiovascular disorders could be missed because administrative data is known for low sensitivity.(Miller et al., 2003; Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999) Administrative data, as opposed to clinical chart review, may lack relevant clinical information which may be important for risk adjustment. (Miller et al., 2003; Romano and Mark, 1994; Iezzoni, 1997; Schwartz et al., 1999)

The temporal relationship issue has to be considered when looking at the association between trauma and acute myocardial infarction. Although we found that certain types of trauma may increase risk of heart attack, there is a possibility that acute myocardial infarction, due to its clinical symptoms, may itself result in trauma. Some case reports, due to the mechanism of injury itself, exclude the possibility of acute myocardial infarction to be the cause of trauma. For instance, Ledley et al.(Ledley et al., 1992) described a man who was hit by a ski lift while getting down from a mountain. Another case when trauma was unlikely to precede the episode of acute myocardial infarction was described by Stewart.(Stewart, 1967) In this case, the traumatic agent

was presented by a piece of wood that kicked upper left quadrant of abdomen and the lower left side of the chest.(Stewart, 1967) The summary of such reports is presented in Table 1.

Some other studies established a clear time interval between trauma and acute myocardial infarction. In such studies, time interval ranged from 1.5 hours to 17 days. The summary of such reports is presented in Table 2.

Some reports aimed to exclude patients with unclear presentation whether trauma preceded or followed acute myocardial infarction(Moosikasuwan et al., 2000) even though the evidence from those patients who were included into this study was sometimes based on verbal denial of symptoms of acute myocardial infarction before trauma.

Finally, there are reports which present patients that were injured in a motor-vehicle crash and the description of study either lacks the information on the patient clinical symptoms that immediately preceded the episode of injury or the patient was delivered with loss of consciousness. The summary of such reports is presented in Table 3.

In general, such bi-directional association between trauma and acute myocardial infarction should be thoroughly studied in longitudinal studies with in-depth clinical information, possibly from clinical charts.

5.3. PUBLIC HEALTH IMPORTANCE: THE ATTRIBITABLE RISK FOR CARDIOVASCULAR DISEASES DUE TO INJURIES

Both injuries and cardiovascular diseases are important public health problems. Injuries, for instance, remain the leading cause of disabilities in the US.(MacKenzie, 2000) They are the leading cause of death among young Americans.(MacKenzie, 2000) At the same time, one fifth of the US population has experienced some kind of cardiovascular disease. (Lefkowitz and Willerson, 2001) Almost one million Americans die because of cardiovascular disorders every

year.(Lefkowitz and Willerson, 2001) Hundreds of billion dollars are spent annually to treat heart and vascular problems.

We estimated the attributable risk for myocardial infarction due to trauma based on our findings. The age-adjusted rates of acute myocardial infarction based on hospital discharges have been established elsewhere.{McGovern, Jacobs, et al. 2001 #3440} Among men 30 to 74 years, such rate is 4.12 per 1,000 while for women it is 1.48 per 1,000. The number of blunt cardiac injury (BCI) based on hospital discharges that include all ICD-9 codes is 5,418, while such numbers for abdominal and pelvic trauma and for thoracic trauma are 68,714 and 114,540 accordingly.

Because we have obtained different odds ratios depending on coronary arteriography status and age group, our estimates for BCI among men would be in a range from 31 to 701, while for abdominal and pelvic injury such estimates among men would be in a range from 467 to 1791. For thoracic injury, the number of additional cases of acute myocardial infarction among men would be 585. Therefore, depending on arteriography status and age group, the number of additional cases of acute myocardial infarction among men due to trauma ranged from 1,083 to 3,077.

Among women, our estimates for BCI would be in a range from 12 to 252, while for abdominal and pelvic such estimates would be in a range from 168 to 643. For thoracic injury, the number of additional cases of acute myocardial infarction among men would be 211. Therefore, depending on arteriography status and age group, the number of additional cases of acute myocardial infarction among women due to trauma ranged from 391 to 1106.

However, there are several issues which must be considered when calculating the attributable risk for cardiovascular diseases due to injuries. There might be a higher probability

of sustaining blunt cardiac injury in the presence of pre-existing valvular or ischemic heart disease. Such probability may have been higher because cardiac tissues may have been weakened due to the effects of chronic dilation and hypertrophy such that compression of the cardiac chambers and increase of intracardiac pressure from injury forces were particular significant.

On the other hand, pre-existing cardiac valvular disease might lead to a higher likelihood of the diagnosis of blunt cardiac injury being made however administrative databases provide only limited insight into this issue since acceptance of a very specific diagnosis varies not only among hospitals but also across physicians.

Also, as we have mentioned, ICD-9-CM coding did not allow us to differentiate cardiac valve insufficiency from cardiac valve stenosis (codes 424.1 – 424.3) except in the case of mitral valve insufficiency and regurgitation (code 424.0). Therefore, some of the identified cases may have been diagnosed with cardiac valve stenosis, which has not been shown to be associated with injury.

Therefore, longitudinal studies based on medical chart review would provide more definitive answers with regard to attributable risk for cardiovascular diseases due to trauma. Such studies would provide better insight into timing of events, while charts review may provide more detailed clinical information on such asymptomatic outcome as for instance cardiac valve insufficiency.

Although, based on our results, trauma may represent a small attributable risk for cardiovascular diseases, however, our current estimation of the burden of cardiovascular diseases from injuries may be greatly undermined because we took into account only hospitalized cases of

both exposure and the disease without looking the follow up outcomes. In addition, we have not looked at those cases of injuries that resulted in death before or during the hospitalization.

5.4. PUBLIC HEALTH AND CLINICAL IMPLICATIONS

Evidence provided by the improvement in motor-vehicle safety, helmet law enforcement and various behavioral interventions has shown that injuries are preventable. Moreover, preventive strategies have been implemented to reduce the burden from cardiovascular diseases. In the 21st century, new technologies provided researchers with the opportunities to understand the molecular and genetic basis for various cardiovascular disorders yet, delineation of new risk factors for heart and vascular diseases remains a key strategy for future prevention in this area.(Lefkowitz and Willerson, 2001)

It is important to firm and quantify the association between trauma and cardiovascular disorders because treatment strategies in the case of traumatic cardiac disorders may be different from those that are usually undertaken in the case of non-traumatic cardiovascular disorders. Cardiac valve disorders are often asymptomatic conditions which, if left untreated, may lead to various cardiac and non-cardiac complications. For example, in the case of traumatic cardiac valve insufficiency, early and specific surgical treatment (i.e. valve replacement (Anyanwu, 1976; Bryant et al., 1973) and annuloplasty(Chang et al., 1989)) is often a necessity while in case of non-traumatic cardiac disorders treatment is usually directed toward the underlying cause of valve disorder.

Thrombolytic therapy is problematic in the trauma victims with head trauma or multiple injuries, indeed, there has been only one report showing successful use of thrombolytic therapy.(Ledley et al., 1992) Effective treatment might include strategies to prevent hyperviscosity and rouleaux formation that might be one of the key pathophysiological

components of traumatic myocardial infarction.(Ismailov, 2005) The suggestion that increased blood viscosity may be a contributing mechanism might advocate the therapy that is directed toward improving blood rheology. Because some patients with traumatic myocardial infarction may also develop aneurismal disease(Ginzburg et al., 1998), early surgical treatment may be a necessity as well.

About half a million deaths in the US are attributed to serious cardiac arrhythmias. (Anonymous2000) Ventricular paroxysmal tachycardia, if not timely treated, can degenerate spontaneously into ventricular fibrillation or may result in congestive heart failure.(Stewart et al., 1986; Anonymous2000)

In the case of traumatic cardiovascular disorders, such preventive strategies may range from relatively inexpensive diagnostic procedures such as auscultation and ECG to advanced and expensive invasive cardiac procedures such as cardiac catheterization. For example, various cardiac valvular disorders could be diagnosed by proper auscultation, where a systolic murmur suggesting mitral incompetence could be heard with no additional cardiac symptoms. However, Echocardiography with Doppler is considerably more accurate as a diagnostic tool. (Ganz and Friedman, 1995) While some authors suggest auscultation immediately following by echocardiography in the trauma patients, the future studies should focus on most effective and clinically proven diagnostic procedures that will help to prevent cardiac valve insufficiency caused by trauma.(Ganz and Friedman, 1995) In the case of acute myocardial infarction, an early diagnosis which often can be made using ECG may not only significantly improve the outcome (i.e. decrease the area of myocardial necrosis) but also prevent certain complications such as ventricular fibrillation and cardiac arrest. In addition, cardiac arrhythmias are often being asymptomatic and can only be diagnosed if certain test, most often, ECG is administered. For

instance, supraventricular paroxysmal tachycardia, often being asymptomatic, may cause pulmonary edema or myocardial ischemia. (Ganz and Friedman, 1995)

For the first time in the literature, we found that abdominal and pelvic traumas may increase risk of acute myocardial infarction. Abdominal trauma is particularly dangerous among children where the mortality could be as high as 8.5%. (Bergqvist et al., 1985) Among adults it is often associated with bicycle accidents(Bergqvist et al., 1985) but unusual events such a blunt stab from the end of a stick in a hockey(Zaunschirm and Steiner, 1989)and from a football(Lyons, 1992). On the other hand, a number of complications have been associated with pelvic trauma while we report an association between pelvic trauma and acute myocardial infarction. Usually pelvic trauma results from motor vehicle accidents, falls and crush injuries.(Ferrera and Hill, 1999) Pelvic trauma may have a mortality rate as high as 30%. (Wubben, 1996)

Our finding that abdominal or pelvic trauma may increase risk of acute myocardial infarction may further justify the development and improvement the existing protection devices that are aimed to protect abdominal and pelvic area such as abdominal pads. On the other hand, it is the weakened, due to aging, abdominal muscles or pelvic ligaments that may result in significant compression, resulting blood deceleration and increase of intravascular hydrostatic pressure. Therefore, strengthening abdominal and pelvic muscles may possibly result in decrease risk of acute myocardial infarction in case of injury.

5.5. FUTURE IMPLICATIONS

We are hoping to conduct longitudinal studies to address those limitations that we have encountered in cross-sectional studies. Prospective studies are needed:

1.   To broaden knowledge about the temporal relationship between certain cardiac events such as acute myocardial infarction and trauma.

2.   To clarify whether patients with traumatic cardiovascular diseases are more likely to develop further complications (i.e. congestive heart failure, pulmonary edema, cardiogenic shock) compared to patients with non- traumatic cardiovascular diseases.

3.   To evaluate the possible superimposition of various traumatic cardiovascular events such as traumatic arrhythmias on cardiac valve insufficiency or overall survival.

4.   To study the association between traumatic myocardial infarction and pre-existing coronary heart disease.

One of the sources of data of such longitudinal studies is a linkage of the existing hospital discharge data. The other sources of data for the prospective studies are police certificates and medical charts from emergency rooms. Outcomes of such studies (i.e. deaths and incidence of traumatic cardiovascular events) should be related to demographic data, various injury characteristics, and previous history of cardiovascular diseases. A prospective protocol should include patients identified through emergency department who suffered clinical evidence of blunt cardiac, thoracic, abdominal and pelvic injuries. Other injuries of interest might include back, spine trauma, and, if proper mechanism will be established, traumatic brain injury. Various diagnostic tests identified through a detailed literature review should be performed at the baseline and follow up. While patients will be at the hospital (i.e. emergency department), a follow-up evaluation should be accompanied through daily review of medical charts. All surgical procedures, cardiac events and all other interventions should be documented. After hospital

discharge, data will be obtained during follow up visits and through communication with the family physician. The availability of Holter monitoring on hospital admission should serve as one of the criterion when identifying the appropriate emergency department for the prospective study. Certain patients should be excluded from the study such as with ischemic heart disease, rhythm disturbances, cardiac surgery, congestive heart failure. Such exclusion can be made by the physician at the emergency room. Detailed information on accident history to estimate whether low- or high- energy transfer was involved in the trauma mechanism should be made. A common problem with cohort method, namely a long follow up period can be avoided if various cardiovascular events should be included. In addition, to avoid a long follow up in a control group, the recorded disease rates from national estimates may be used.

6. CONCLUSIONS

With the findings that several types of injury such as thoracic, cardiac, abdominal and pelvic are associated with an increased risk of specific cardiovascular disorders – namely – cardiac valve insufficiency, acute myocardial infarction and cardiac arrhythmias, it is possible that trauma may play an important and heretofore largely unrecognized role in a portion of the burden of cardiovascular morbidity and mortality. Thus, the burden of injury on the broad spectrum of clinical outcomes may be under-estimated if relevant conditions are ignored.

APPENDIX A

Trauma associated with acute myocardial infarction: the possibility of bi-directional relationship

Table 13 Summary of studies where trauma preceded the episode of acute myocardial infarction due to mechanism of injury

	Author	Age	Mechanism of injury
1.	Atalar et al. (Atalar et al., 2001)	22	Hit in the chest by a soccer ball
2.	Dahle et al. (Dahle et al., 2005)	35	Hit by the other player's elbow during soccer game
3.	Darok et al. (Darok et al., 2001)	28	Hit in the chest by a wooden wheel of a lifting machine
4.	DeFeyter et al. (de Feyter and Roos, 1977)	36	Struck in chest by football ball
5.	Espinosa et al. (Espinosa et al., 1985)	33	Hit by soccer ball
6.	Jokl et al. (Jokl and Greenstein, 1944)	10	Struck in chest during box match
7.	Jones et al. (Jones, 1970)	13	Swept from horse by tree limb
8.	Jessurun (Jessurun et al., 1996)	46	Hit in the chest by a soccer ball
9.	Harthorne et al. (Harthorne et al., 1967)	32	Struck in chest during barroom brawl
10.	Heymann et al. (Heymann and Culling, 1994)	42	Struck on the chest by the cricket ball
11.	Marcum et al. (Marcum et al., 1996)	44	Struck by a horse's hoof
12.	Moore et al. (Moore, 2001)	30	Hit by basketball ball
13.	Motro et al. (Motro et al., 1981)	11	Hit by basketball ball
14.	Ledley et al. (Ledley et al., 1992)	34	Hit in the chest by a ski lift
15.	Lee et al. (Lee et al., 1991)	29	Hit in the chest by umbrella tip
16.	Lin et al. (Lin et al., 2004)	23	Struck by a ball by a basketball ball
17.	Oren et al. (Oren et al., 1976)	35	Struck in chest by fist
18.	Rab et al. (Rab, 1969)	27	Hit by cricket ball
19.	Stewart et al. (Stewart, 1967)	42	Struck by piece of wood recoiling from circular saw

Table 14 Summary of studies where time interval between trauma (motor vehicle crash) and acute myocardial infarction was established by authors

	Author	Age	Mechanism of injury	Time interval between trauma and acute myocardial infarction
1.	Banzo et al. (Banzo et al., 1999)	30	Motor vehicle crash	20 hours
2.	Boland et al. (Boland et al., 1988; Banzo et al., 1999)	32	Motor vehicle crash	4 days
3.	Candell et al. (Candell et al., 1979)	38	Motor vehicle crash	24 hours
4.	Foussas et al. (Foussas et al., 1989)	26	Motor vehicle crash	17 days
5.	Lee et al. (Lee et al., 1990)	54	Motor vehicle crash	3 days
6.	Lehmus et al. (Lehmus et al., 1954)	62	Motor vehicle crash	1.5 hours
7.	Oliva et al. (Oliva et al., 1979)	44	Motor vehicle crash	24 hours
8.	Vlay et al. (Vlay et al., 1980)	25	Motor vehicle crash	5 days

Table 15 Summary of studies where patients were presented with the clinical picture of acute myocardial infarction upon admission to the hospital following the episode of trauma

	Author	Age	Mechanism of injury
1.	Chun et al. (Chun et al., 1998)	17	Fell of bicycle
2.	Foussas et al. (Foussas et al., 1989)	47	Fell from height
3.	Gaspard et al. (Gaspard et al., 1983)	21	Motor vehicle crash
4.	Heyndrickx et al. (Heyndrickx et al., 1974)	62	Motor vehicle crash
5.	Kahn et al. (Kahn and Buda, 1987)	30	Motor vehicle crash
6.	Kohli et al. (Kohli et al., 1988)	38	Motor vehicle crash
7.	Lascault et al.(Lascault et al., 1986)	28	Fell from height
8.	Oliva et al. (Oliva et al., 1979)	44	Motor vehicle crash
9.	Park et al. (Park et al., 2003)	16	Motorcycle crash
10.	Pifarre et al. (Pifarre et al., 1982)	58	Motor vehicle crash
11.	Pifarre et al. (Pifarre et al., 1982)	20	Motor vehicle crash
12	Pringle et al. (Pringle and Davidson, 1987)	20	Motor vehicle crash
13.	Rab et al. (Rab, 1969)	38	Motor vehicle crash
14.	Shapiro et al. (Shapiro et al., 1994)	23	Motor vehicle crash
15.	Stern et al. (Stern et al., 1974)	16	Motor vehicle crash
16.	Unterberg et al. (Unterberg et al., 1989)	38	Motor vehicle crash

APPENDIX B

Mathematical model of blunt injury to the vascular wall via formation of rouleaux and changes in local hemodynamic and rheological factors. Implications for the mechanism of traumatic myocardial infarction.

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Abstract

Background. Blood viscosity is fundamentally important in clinical practice yet the apparent viscosity at very low shear rates is not well understood. Various conditions such as blunt trauma may lead to the appearance of zones inside the vessel where shear stress equals zero. The aim of this research was to determine the blood viscosity and quantitative aspects of rouleau formation from erythrocytes at yield velocity (and therefore shear stress) equal to zero. Various fundamental differential equations and aspects of multiphase medium theory have been used. The equations were solved by a method of approximation. Experiments were conducted in an aerodynamic tube.

Results. The following were determined: (1) The dependence of the viscosity of a mixture on volume fraction during sedimentation of a group of particles (forming no aggregates), confirmed by published experimental data on the volume fractions of the second phase (f_2) up to 0.6; (2) The dependence of the viscosity of the mixture on the volume fraction of erythrocytes during sedimentation of rouleaux when yield velocity is zero; (3) The increase in the viscosity of a mixture with an increasing erythrocyte concentration when yield velocity is zero; (4) The dependence of the quantity of rouleaux on shear stress (the higher the shear stress, the fewer the rouleaux) and on erythrocyte concentration (the more erythrocytes, the more rouleaux are formed).

Conclusions. This work represents one of few attempts to estimate extreme values of viscosity at low shear rate. It may further our understanding of the mechanism of blunt trauma to the vessel wall and therefore of conditions such as traumatic acute myocardial infarction. Such estimates are clinically significant, since abnormal values of blood viscosity have been observed in many

pathological conditions such as traumatic crush syndrome, cancer, acute myocardial infarction and peripheral vascular disease.

Introduction

Blood is a liquid-liquid suspension because erythrocytes exhibit fluid-like behavior under certain shear conditions [1]. The dependence of viscosity on shear rate is one of the most widely used rheological measurements [2]. Normal blood also thins when it is sheared, therefore its apparent viscosity is highly sensitive to shear rates below 100 s^{-1} [2,3].

The objective of this research was to determine blood viscosity at yield velocity (and therefore shear stress) equal to zero. Our previous studies have shown that conditions such as blunt trauma to large vessels may lead to boundary layer separation where du / dy = 0, i.e. to the appearance of zones where shear stress equals zero [4]. A further aim of this research was to evaluate quantitative aspects of rouleau formation from erythrocytes when the yield velocity is equal to zero.

Methods

Various calculations have been made for the viscosity of a mixture and the coefficient of constraint [5-7]. There is considerable variation in such calculations, resulting from different combinations of phases. This variation apparently reflects the non-Newtonian nature of concentrated viscous disperse mixtures and the insufficiency of the variables ρ and μ alone (where ρ is density and μ is viscosity) to determine the mechanical properties of such mixtures. In this regard, experiments over the range of operating parameters are needed for any mixture to determine pressure loss using different rheological models; in particular, the model of a viscous

fluid with an effective viscosity coefficient. It must be noted that when $f_2 > 0.1$ (where f_2 is the volume fraction of the second phase), not only the shape and size of the erythrocytes but also the irregular arrangement of the particles and their collisions with each other and with the solid walls have substantial effects on the effective viscosity and other rheological characteristics of the mixture [8,9].

The problems mentioned above have led to studies of group sedimentation at $f_2 > 0.1$ in the interpenetrating model of two- or multi-phase media [10]. These studies usually deal with either high- or low-concentration mixtures. Mechanisms of sedimentation in moderately concentrated mixtures, which are rather common, have not been fully investigated. Mathematical modeling of group sedimentation of particles (in our case, rouleaux) in two-phase interpenetrating media [11] should take into account not only the Stokes force [12] but also other forces that are given in [13]:

$$F_{12}{}^{(A)} = -f_2 \Delta p$$

$$F_{12}{}^{(\mu)} = -f_2 \rho_1{}^0 K^{(\mu)} (u_1 - u_2)$$

$$K^{(\mu)} = K^{(\mu)} (f_2 |u_1 - u_2|, \mu_1, \mu_2, a, ...) \tag{1}$$

$$F_{12}{}^{(m)} = f_2 \rho_2{}^0 \chi^{(m)} \left(\frac{du_1}{dt} - \frac{du_2}{dt} \right)$$

$$F_{12}{}^{(r)} = f_2 \rho_1{}^0 \chi^{(r)} (u_1 - u_2) \cdot rot u_1$$

where $F_{12}{}^{(A)}$ is a buoyancy force, Δp- pressure difference, $\chi^{(m)}$- coefficient of constraint, ρ- density of the first phase, $K^{(\mu)}$ – coefficient of phase interaction, μ_1 and μ_2 – viscosities of the first and second phases, f_2 – the volume fraction of the second phase. It is also important to calculate μ, the viscosity of the blood mixture, which depends on the volume fraction of particles. In this

case it is possible to determine the force $F_{12}{}^{(\mu)}$. $F_{12}{}^{(\mu)}$ is a frictional force or Stokes force that results from viscous forces involved in the interaction between phases. $F_{12}{}^{(\mu)}$ is calculated using the difference between velocities (slippage) u_1 - u_2, the particle size a, the quantities and shapes of inclusions, and the physical properties of the phases (see equation 1). (The effects of the shape and multiplicity of particles, and of some other variables included in the expression for $F_{12}{}^{(\mu)}$, are accounted for in coefficients $K^{(\mu)}$ in (1)).

Using all of the above, I shall determine blood viscosity as a variable dependent on a volume fraction of particles. This will allow me to determine blood viscosity at a yield velocity of zero, and the number of rouleaux as a variable dependent on erythrocyte concentration, shear stress and yield velocity.

Determination of viscosity of a mixture as a variable dependent on volume fraction of particles

Sedimentation of a single particle is based on the Stokes law, according to which a frictional force resulting from the motion of spherical particles with diameter d and velocity V in a medium of viscosity μ is expressed by the equation:

$$F_{12}^{(M)} = 6\pi\mu a V \tag{2}$$

where a – radius of particles (inclusions) and V – velocity of particle precipitation.

In the general case of a multiphase medium, the frictional force or Stokes force $F_{12}{}^{(\mu)}$, which results from viscous forces involved in the interactions between phases, is calculated using the difference between velocities (slippage) u_1 - u_2, the particle size a, the quantity and shape of inclusions, and the physical properties of the phases.   Multiphase models are based on the idea of interpenetrating media, where the system of particles is replaced by a mathematical

continuum and particle size is considerably less than the distance over which flow conditions may change [11].

The force of gravity acting on a particle is calculated using the specific gravity of the particle; that is:

$$F_{12}^{(A)} = \frac{\pi}{6} d^3 (\rho_2 - \rho_1) g \qquad (3)$$

where $\rho_1; \rho_2; g$ are respectively the density of the fluid, the density of the particle, and the acceleration due to gravity.

$F_{12}^{(A)}$ is a buoyancy force (Archimedes force);

$F_{12}^{(M)}$ is a frictional force or Stokes force.

Force $F_{12}^{(A)}$ causes a particle to accelerate. In addition to gravity, the particle is affected by the frictional force, which acts in the opposite direction and has a value directly proportional to the velocity according to the Stokes law. This means that force $F_{12}^{(M)}$ and gravity $F_{12}^{(A)}$ tend to cancel each other out. Therefore, the motion proceeds with a constant velocity V that can be determined from equations (2) and (3):

$$Vs = \frac{(\rho_{2-}\rho_1) g}{18\mu} d^2 = \frac{2(\rho_{2-}\rho_1) g}{9\mu} a^2; \qquad (4)$$

where Vs - velocity of precipitation of a single particle.

Sometimes investigators have to deal with the sedimentation of multiple particles in concentrated mixtures. Formulae for the velocity of sedimentation of particles, dependent on the concentration and velocity of a single particle in an infinite fluid, can be derived using statements from the interpenetrating model [13] and the Euler equation [14]. Assuming that a specific

124

volume has two phases differing in specific gravity, the particles with the greater specific gravity will start moving down a channel, so that a process of mutual penetration occurs.

The flow of the fluid can be expressed by criterion equations:

$$E_u = AR_e^m \left(\frac{1}{d_e} \right)^n$$

where E_u – Euler number, A – coefficient of proportionality, R_e – Reynolds number; or:

$$\frac{\Delta p}{\rho_1 V_1^2} = AR_e^m \left(\frac{1}{d_e} \right)^n$$

In the process of sedimentation when the concentration of inclusions is rather high and the particle size is small, flow is laminar; m = - 1 and n = 1 (where m and n are criterion coefficients).

Taking into account data from [13]:

$$S_i = \frac{6f_2}{d}$$

(5)

$$d_e = \frac{2}{3} \frac{f_1 d}{f_2}$$

where S_i – particle surface area; f_1 – volume fraction of the first phase; f_2 – volume fraction of the second phase

Dividing the continuity equation:

$$V_1 S = V_{1i} S_1$$

by S, I obtain:

$$V_1 = f_1 V_{1i} \tag{6}$$

where S is the area of the canal section.

Therefore:

$$\frac{\Delta P}{\rho_1 V_1^2} = \frac{A\mu l}{\rho_1 d_e^2 V_1}$$

Using equations (5) and (6), I can transform the last equation into the Kozeny-Carman formula for restrained sedimentation in a laminar flow:

$$F = \frac{9 A V_1 \mu f_2^2}{4 f_1^3 d^2} \tag{7}$$

where A lies within the range 80-110.

Dividing equation (7) by the number of particles per unit of volume allows the resistance force applied by the fluid to a single particle to be derived as:

$$F^* = \chi \frac{\pi \rho V^2 d^2}{f_1^3} \tag{8}$$

Where F^* – resistance force created by the fluid and acting on a single particle, and χ – coefficient of resistance for precipitation of multiple particles.

The resistance force applied to a single particle during precipitation in a fluid is known to be [12,15]:

$$F_c = \chi_c V_c^2 d^2 \rho \tag{9}$$

For particles suspended in a fluid:

$$F^* = F_{12}$$

therefore from (8) and (9) it follows that:

$$\chi = \frac{f_1^3}{\pi\beta^2}\chi_c; \tag{10}$$

where β – the ratio of the velocity of sedimentation of the group of particles to the velocity of sedimentation of a single particle, and χ_c – the coefficient of resistance when precipitating a single particle in an infinite fluid.

From (10), when $f_1 \to 1$ it follows that:

$$\chi = \frac{\chi_c}{\pi}$$

when the Reynolds numbers are small:

$$\chi = \frac{c}{\text{Re}}$$

where c – constant.

Therefore, it can be assumed that:

$$\chi = \frac{c}{\text{Re}} + \frac{\chi_c}{\pi} \tag{11}$$

From equations (10) and (11) it follows that:

$$\beta = -3c\frac{\pi f_2}{\text{Re}_c\,\chi_c} + \left[\left(3c\frac{\pi f_2}{\text{Re}_c\,\chi_c}\right)^2 + f_1^3\right]^{\frac{1}{2}}, \tag{12}$$

where:

$$\text{Re}_c = \frac{V_c d}{\nu}$$

where ν – the coefficient of viscosity.

When the motion is laminar, according to the Stokes law:

$$\chi_c = \frac{3\pi}{\text{Re}_c}$$

Substituting this expression in equation (12), it follows that:

$$\beta = -c\,f_2 + [c^2(1 - f_1)^2 + f_1^3]^{\frac{1}{2}} \tag{13}$$

If one considers the sedimentation of a particle in a suspension with viscosity μ_m and density ρ_m, then the equilibrium equation [13] can be expressed as:

$$f_2 \rho_{2i} g - f_2 \rho_m g + \frac{9}{2} f_2 \mu_m a^{-2} (V_1 - V_2) = 0 \tag{14}$$

$$V_c = \frac{2}{9} \frac{(\rho_2 - \rho_1) g}{\mu_1} a^2 \tag{15}$$

$$\rho_m = f_1 \rho_{1i} + f_2 \rho_{2i} \tag{16}$$

Using equations (14), (15) and (16) and the condition $V_1 = 0$ it follows that:

$$\frac{\mu_m}{\mu_1} = \frac{f_1 V_c}{V_2} \tag{17}$$

Substituting the relative velocity equation (13) into equation (17), it follows that:

$$\frac{\mu_m}{\mu_1} = f_1 \Big/ \left(\sqrt{c^2(1 - f_1)^2 + f_1^3} - cf_2 \right) \tag{18}$$

When $f_1 \to 1$ and $c = 2.5$, this reduces to the Einstein formula:

$$\frac{\mu_m}{\mu_1} = 1 + cf_2 \tag{19}$$

From the calculation given in Figure 1, it follows that equation (18) is consistent with the experimental data (up to $f_2 = 0.5$ when $c = 2.5$) obtained by other investigators [6,7] regarding the velocity changes in suspensions for a wide range of fluids and particle sizes as well as particle compositions. Figure 2 shows the relationship between relative sedimentation velocity and particle concentration. The relationship between relative velocity, viscosity and volume fraction is also consistent with experimental data [6,7].

Determination of viscosity when yield velocity equals zero

The value of viscosity derived in equation (18) describes the sedimentation of solid particles, that is particles that do not form rouleaux. I shall now determine the viscosity of blood when the yield velocity is zero. It is known [16] that if whole blood (in which coagulation is prevented) is placed in a vertically-positioned capillary tube, erythrocytes will aggregate into rouleaux and then sediment. Therefore the viscosity μ_1 must be determined in blood that has minimal numbers of rouleaux, and it is necessary to take into account the effect on rouleau sedimentation of erythrocytes that remain suspended . Such a condition occurs when the yield velocity is high $(500 - 1000 \text{ s}^{-1})$ and the number of rouleaux is minimal. This condition can be expressed by equations (18) or (19) when $f_1 \to 1$ and $c = 2.5$; that is rouleaux do not sediment in plasma but rather in a mixture of erythrocytes, plasma and a certain number of rouleaux.

Calculations made according to equations (18) or (19) when $f_1 \to 1$ and $c = 2.5$ yield the following results:

$\mu_1 = 6.8 \text{ mNsm}^{-2}$ when concentration of erythrocytes is 28.7%

$\mu_1 = 8.8 \text{ mNsm}^{-2}$ when concentration of erythrocytes is 48%

$\mu_1 = 10$ mNsm^{-2} when concentration of erythrocytes is 58.9%

These data are consistent with experimental data [16] when the yield velocity ranges from 500 to 1000 s^{-1}. Thus, using the effect of the viscosity of the mixture from equations (18) and (19), I can calculate the viscosity of the blood at zero velocity by means of the following equation:

$$\mu_m = ((1 + cf_2)\mu_1 f_1 / (\sqrt{(c^2(1 - f_1)^2 + f_1^3)}) - cf_2)$$

(20)

In this equation, when coefficient $c = 2.5$, there is a minimal number of rouleaux at $\mu_1 = 3$ to 4 mNsm^{-2} (the value of viscosity when the maximum yield velocity is more than 500 s^{-1}). Figure 3, where the viscosity at zero yield velocity is plotted on the Y axis, shows that viscosity increases with increasing concentration. Thus an increase in erythrocyte concentration results in an increase of viscosity.

I shall now determine the shear stress at various concentrations and yield velocities. Table 1 shows that an increase of shear stress causes a decrease of viscosity. Thus, an increase in the concentration of erythrocytes will result in an increase of viscosity and a decrease in shear stress. It can be assumed that a maximal number of rouleaux is formed when the yield velocity is zero, since there are no forces that disassemble them. Then I can determine the number of rouleaux at different values of viscosity and shear stress. Table 2 shows these data and indicates that the main source of rouleaux is the erythrocytes themselves. The higher the erythrocyte concentration, the more rouleaux remain in the blood despite an increase in the forces that destroy them. It is also clear that an increase in shear stress results in a decrease of the number of rouleaux.

I can now determine the concentration of rouleaux, assuming that viscosity is determined by the numbers of erythrocytes only at a high yield velocity (since high yield velocities destroy

rouleaux). Granted this assumption, the viscosity is determined according to the Einstein equation (18) and (19). Viscosity at decreasing yield velocity is determined by both erythrocytes and newly-formed rouleaux. Then, according to equation (20), I obtain the result presented in Figure 4: the number of rouleaux decreases sharply with increasing yield velocity. Therefore, the number of rouleaux depends on the concentration of erythrocytes.

The quantity of rouleaux depends on shear stress (the higher the shear stress, the lower the rouleaux content of the blood) and erythrocyte concentration (the more erythrocytes, the more rouleaux will be formed). I can now determine whether all rouleaux are interconnected and what kind of cohesive forces operate among them. It is known that at low yield velocities, a greater fraction of the erythrocytes form rouleaux [16]. These long columns of erythrocytes have a certain stiffness and might interweave to form a single structure [16]. It is hypothesized that cohesive forces may vary among rouleaux. This phenomenon makes the properties of blood resemble those of a solid body. When the yield velocity increases, the length of the rouleaux gradually decreases and ultimately only stand-alone erythrocytes are left.

To test this hypothesis, an experiment was conducted in which the breaking force and shear stress were those that naturally destroy rouleaux, but the cohesive forces were different. In an aerodynamic tube, a laminar boundary layer was created on a flat surface with the required shear stress on the surface of the wall [4]. On this surface, fine particles of equal diameter were placed (the cohesive force ranged from 0.0027 mN to 0.035 mN). From this information I could determine the destruction, i.e. the detachment and separation of particles from the surface. The results of the experiment are given in Table 3.

Table 3 shows that destruction of rouleaux decreases with increasing particle diameter (which means increasing cohesive force). Conversely, the destruction of rouleaux increases with

increasing shear stress. It can be supposed that an increase in shear stress destroys rouleaux that have a cohesive force lower than the breaking force. A further increase in shear stress will lead to the destruction of rouleaux with a greater cohesive force.

Summary of results

The following have been determined:

1. The dependence of the viscosity of a mixture on volume fraction during sedimentation of a group of particles (forming no aggregates), confirmed by published experimental data [7] for volume fractions of the second phase (f_2) up to 0.6.

2. The dependence of viscosity of a mixture on the volume fraction of erythrocytes during sedimentation of rouleaux when the yield velocity is zero.

3. Increase in the velocity of a mixture with an increasing concentration of erythrocytes when yield velocity is zero.

4. An increased erythrocyte concentration results in an increase of viscosity of the mixture, and an increase in shear stress results in a decrease of viscosity of the mixture.

5. The quantity of rouleaux depends on shear stress (the higher the shear stress, the fewer rouleaux in the blood) and erythrocyte concentration (the more erythrocytes, the more rouleaux are formed).

6. With an increase in shear stress, those rouleaux are destroyed whose cohesive force is weaker than the breaking force. A further increase in shear stress will start to destroy rouleaux that have a greater cohesive force.

Discussion

The role of the non-Newtonian viscosity of blood has remained a continuing challenge. Currently, the apparent viscosity at very low shear rates is considered as "effectively infinite immediately before the substance yields and begins to flow" [17]. Traditionally, Casson or Herschel-Bulkley models are used to measure both the yield stress of blood and shear thinning viscosity [18]. Human blood however does not comply with Casson's equation at a very low shear rate [13]. Other attempts to obtain finite viscosity values failed to take into account the hydrodynamic interactions between particles, or the complications related to aggregates [2]. Although an attempt to estimate blood viscosity at a very low shear rate has been made, no study has estimated the viscosity of blood when yield velocity equals zero.

The mathematical model created in this study used the most fundamental differential equations that have ever been derived to estimate blood viscosity. Depending on erythrocyte concentration, this model estimates the blood viscosity at zero yield stress. It takes into account the following factors: (1) Erythrocytes sediment as a group and not as single particles; (2) Erythrocytes interact with each other; (3) Erythrocytes sediment as a rouleaux; (4) Such rouleaux sediment within an erythrocyte-containing medium.

In general, abnormal values of blood viscosity can be observed in such pathologies as cancer [19,20], peripheral vascular disease [19,20] and acute myocardial infarction [19,20]. Blood hyperviscosity may impair the circulation and cause ischemia and local necrosis through decreased capillary perfusion [21]. Blood hyperviscosity due to abnormal red cell aggregation has been found in patients with diabetes, hyperlipidemia and cancer [22]. Estimation of blood viscosity is, however, particularly important in trauma patients. It is known that blunt trauma to vascular walls may lead to conditions for boundary layer separation [4]. Physically, this can be

explained as follows [12]: flow retarded at the surface has low kinetic energy and cannot enter the high pressure zone, therefore it separates from the vessel wall and moves into the inner flow. It should be noted that under normal physiological conditions, the boundary layer does not separate [16]. Shear stress in the zone of boundary layer separation is equal to zero [4]. Therefore, in accordance with the above, trauma may create transient conditions for the formation of rouleaux or for the interlacing of existing rouleaux that have formed in the flowing blood [16], since there is no breaking force at zero shear and yield velocity. A certain number of rouleaux can then enter the arterial branching zone, where the shear velocity and shear stress on the internal wall are low [16], and these rouleaux might attach to the vessel wall, potentially causing atheromatosis. Such arterial branching zones could also be injured by blunt forces, which will also lead to boundary layer separation [4]. Therefore, rouleaux will be formed with low shear velocity and low shear stress on the internal wall [16], also creating conditions for atheromatosis.

Therefore, our understanding of the mechanism of blunt trauma to the vascular wall, which takes into account local hemodynamic and rheological factors, can be summarized in the following way. Trauma leads to the appearance of zones with high shear stress (as the result of injury to part of the vessel) and low or zero shear stress (within the zone of boundary layer separation) [4]. We have reported that high shear stress (exceeding the physiological value) may potentially damage the endothelium [4] and increase platelet aggregation [23,24], possibly leading to thrombus formation. On the other hand, trauma may lead to boundary layer separation, resulting in the appearance of a zone with zero shear stress and zero yield velocity [4]. This may result, according to current research, in an increase of blood viscosity through increased erythrocyte aggregation and rouleaux formation. Such hyperviscosity has been reported in

patients with traumatic crush syndrome and also has been studied in animals exposed to traumatic crush [25]. As noted above, hyperviscosity may worsen the blood circulation and cause ischemia and local necrosis through deterioration in capillary perfusion [21].

This work also establishes a quantitative relationship between the extent of rouleaux formation and shear stress. According to current results, the number of rouleaux increases with decreasing shear stress, and this trend becomes more pronounced as the shear stress approaches zero. Rouleaux continue to form inside what I call the "hemodynamic shade". This "hemodynamic shade" creates a stagnant zone that can be characterized by a secondary flow and a boundary. Hemodynamic stress outside this zone, however, is still significant enough to destroy and entrain rouleaux. The "hemodynamic shade" zone can also be characterized by a significant deterioration of mass exchange due to the attachment of rouleaux to the vessel wall. This may decrease the permeability of the endothelium [16] and decrease the rate of removal of lipids and lipoproteins, which in turn can lead to the formation of lipid stripes directed along the blood flow and located in the "hemodynamic shade" of the original attached rouleaux. The escalating formation of rouleaux continues within the entire "hemodymanic shade" zone.

The model of traumatic damage to the vessel that takes into account local rheological and hemodynamic factors could be applied to many internal injuries involving an elastic vessel wall and a blunt traumatic mechanism. One example is traumatic myocardial infarction, which can result from blunt trauma to the coronary vessels. It should be noted that patients with blunt trauma may develop acute myocardial infarction; such patients may benefit from screening procedures such as electrocardiography, which might improve their chances of survival [8,26-49]. In a large cross-sectional observational study, abdominal, pelvic and blunt cardiac injuries were found to be significantly associated with acute myocardial infarction even after controlling

for confounders such as mechanism and severity of injury, age, sex, race, source of payment, alcohol and cocaine use [50]. Intracoronary thrombosis has been suggested as one of the mechanisms of acute myocardial infarction in young people due to trauma, since other "atherosclerotic" mechanisms do not apply [38,42]. Nonetheless, the exact mechanism of traumatic myocardial infarction remains unclear. Current research suggests that blunt trauma may result in the appearance of a region of very low or zero shear stress, where hyperviscosity and increased rouleaux formation are likely to appear. Large quantities of rouleaux may be transported in the bloodstream toward the more distal parts of the coronary vessels, causing their occlusion. Caimi et al. [51], for instance, observed that blood viscosity at low shear rate is the only hemorheological factor that significantly increases the risk of acute myocardial infarction in young people. On the other hand, blunt trauma may result in traumatic compression of the vessel wall with high shear stress [4]. Increased shear stress itself may cause rupture of a coronary atherosclerotic plaque [52]. In addition, high shear stress may result in increased platelet aggregation [23,24], often leading to thrombus formation.

In summary, there is still a gap in our understanding of all quantitative aspects of the extreme values of viscosity at low and zero shear rates [3]. To the best of my knowledge, the work described in this paper represents one of the few attempts to estimate extreme values of viscosity at low shear rate. An understanding of the precise mechanisms that affect blood viscosity would be of clinical significance.

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Figure 1. The dependence of a change in relative viscosity on the volume fraction of particles
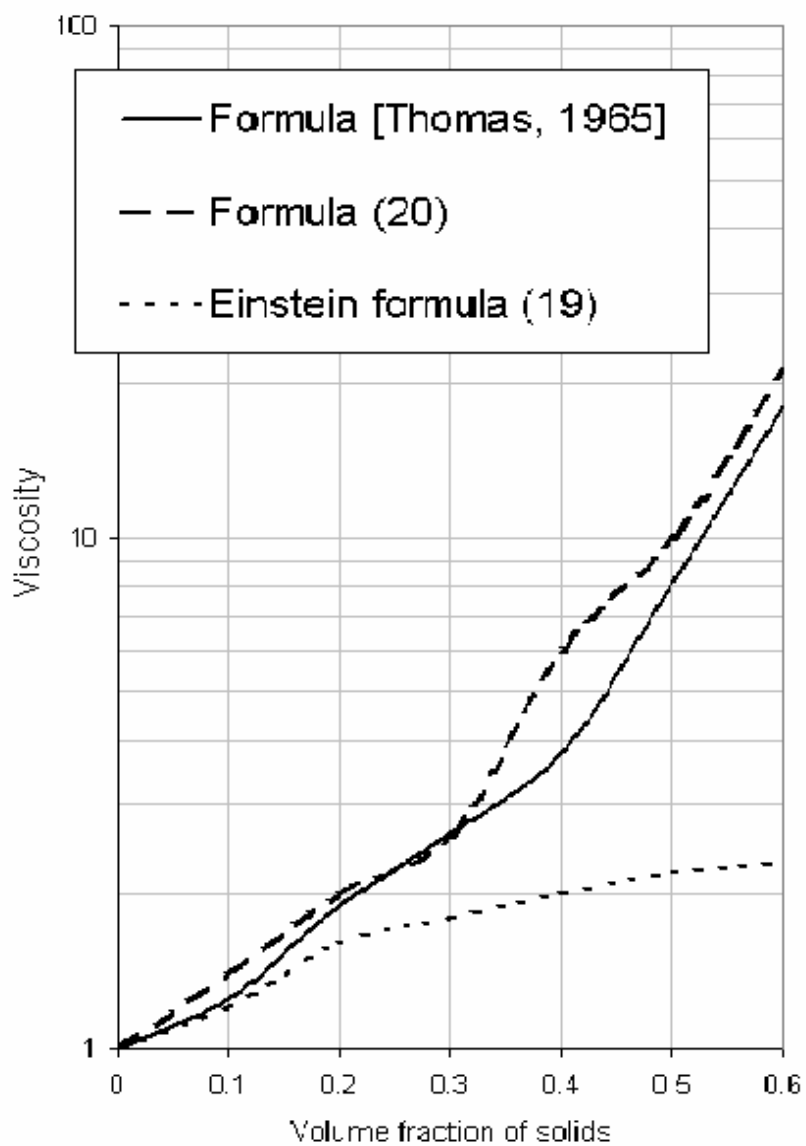
Figure 2. Dependence of relative sedimentation velocity on particle concentration (where β is a change in the relative velocity)
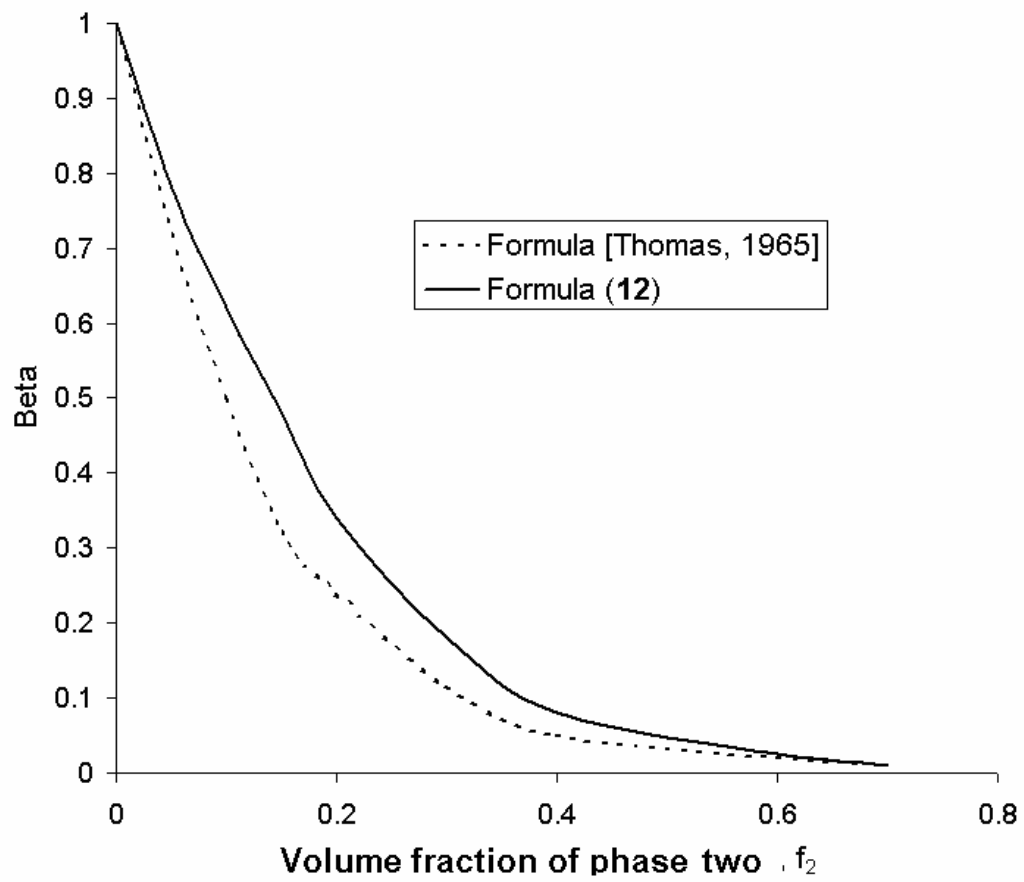
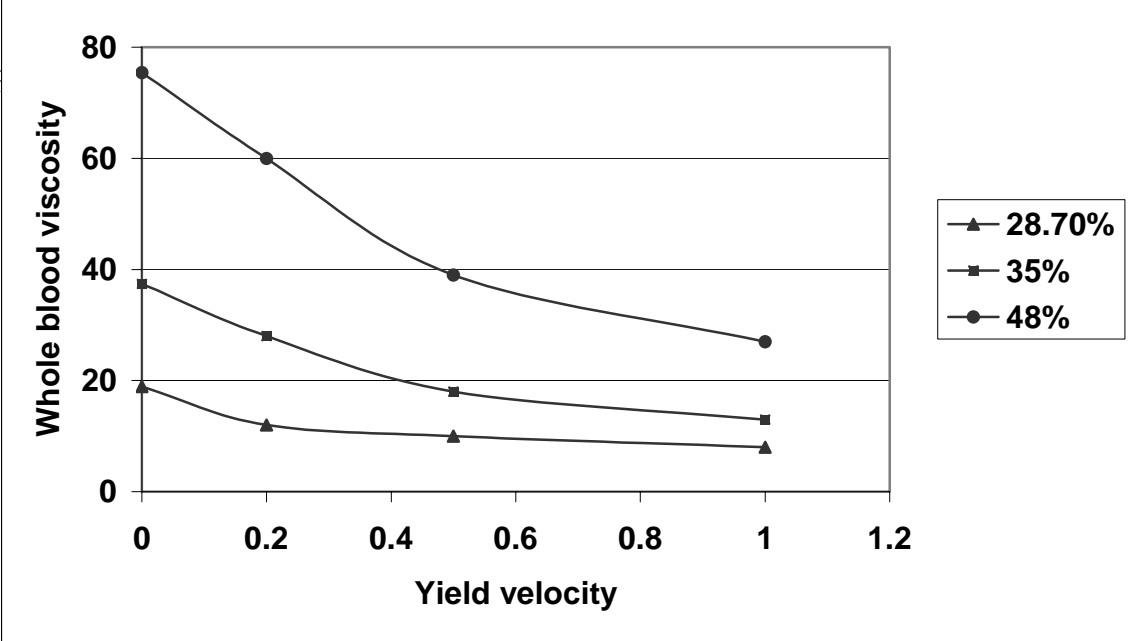Figure 3. The dependence of viscosity on yield velocity

Figure 4. The relationship between the volume fraction of rouleaux and yield velocity
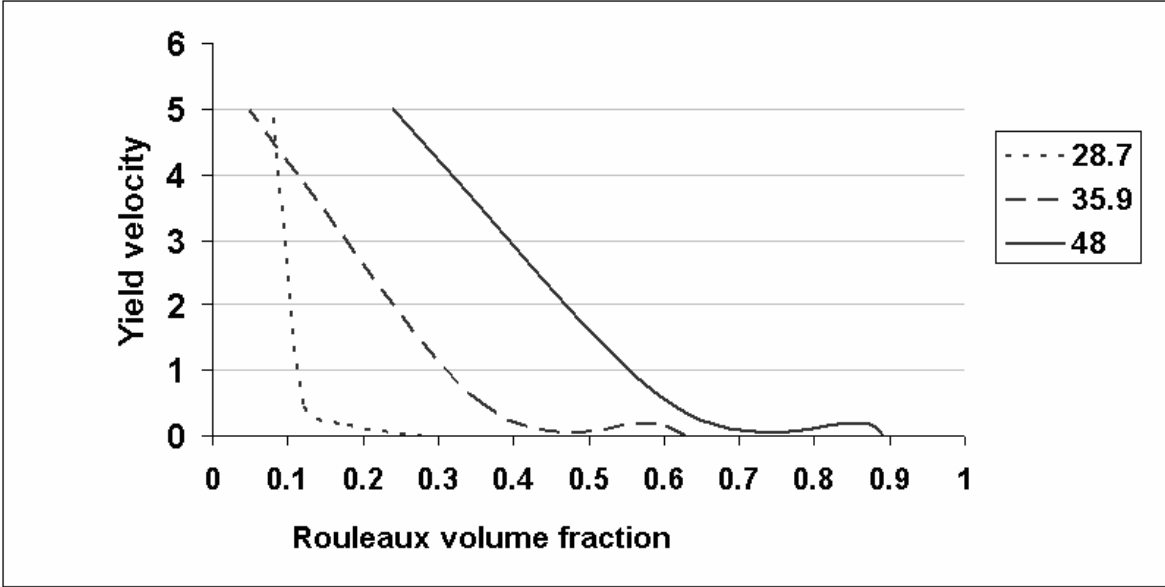
Table 1. Relationship between shear stress and viscosity

Yield velocity (s^{-1})	The volume fraction of the second phase	Viscosity ($mNsm^{-2}$)	Shear stress (N/m^2)
0.2	28.7	13	0.0026
	35.9	30	0.006
	48	63	0.0126
5	28.7	6	0.03
	35.9	8	0.04
	48	15	0.075
100	28.7	4	0.4
	35.9	5	0.5
	48	6	0.6
500	28.7	3	1.5
	35.9	3	1.5
	48	4	2

Table 2. The relationship between erythrocyte concentration and number of rouleaux

Yield velocity (s^{-1})	Concentration %	Viscosity $(mNsm^{-2})$	Rouleaux concentration %	Concentration of destroyed rouleaux %	Shear stress (N/m^2)
0.2	28.7	15	65.2	34.8	0.0026
	35.9	30	81	19	0.006
	48	63	83	17	0.0126
5	28.7	6	26	74	0.03
	35.9	8	21.3	78.7	0.04
	48	15	20	80	0.075

Table 3. The relationship between shear stress, particle diameter and damage to the wall

Shear stress (N/m^2)	Diameter of particles (mm)	Damage (g/s)
0.043	0.25-0.63	0.002
0.051	0.25-0.63	0.03
0.092	0.25-0.63	0.07
0.13	0.25-0.63	0.122
0.13	0.5-0.63	0.05

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