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Acute type A aortic dissection and pregnancy: a population-based study

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Abstract

Objective: Pregnancy has been reported to be an independent risk factor for 50% of acute aortic dissections recorded in women younger than 45 years of age. The present epidemiologic study aimed to identify whether this putative association of pregnancy and acute type A dissection could be an artifact of selective reporting. **Methods:** This population-based study was conducted in the City of Vienna, Austria, Europe, in an average female population of 341 381 women in the age range of 15—45 years who were followed up between 1994 and 2004 (total of 3755.195 person-years of observation). During this study, the incidence, management, and outcome of acute type A dissection were determined. **Results:** Fifteen patients (mean age: 38.8 years, SD: 4.8) with acute aortic dissection were identified, and an overall incidence of 0.4 case per 100 000 person-years was estimated. The prehospital mortality rate was recorded to be 53%. Six patients, including two women in late pregnancy (incidence: 0.05 cases per 100 000 person-years), were treated successfully by surgical repair during deep hypothermic circulatory arrest (in-hospital mortality rate: 6.6%). Pregnancy and aortic dissection were identified as events that were not related (RR: 3.27; 95% confidence interval (CI): 0.82—12.95; $P = 0.14$). Observation during long-term follow-up was uneventful. **Conclusions:** Acute aortic dissection represents a rare pathology in women younger than 45 years of age; however, it is associated with a high rate of sudden death. Pregnancy may not be a risk factor for this life-threatening vascular emergency. Immediate referral to surgery, even during pregnancy, will result in a prognosis of favorable outcome.

Keywords: Aorta; Aortic dissection; Pregnancy; Prognosis

1. Introduction

Acute type A aortic dissection is a potentially lethal cardiovascular emergency [1]. It has been conventionally reported and regularly reiterated in articles and modern textbooks that pregnancy constitutes one of the most important risk factors of acute aortic dissection in women younger than 45 years [2—4].

However, despite the extensive literature available on the management of aortic dissection, the incidence and natural history of this condition have been poorly investigated as yet [5]. Previously, evidence was obtained primarily from case reports and small clinical case series [6—8]; however, newer, more comprehensive clinical information has emerged from multi-center studies based on the study of selected, non-consecutive cases [9—12]. These studies, however, are proved to be non-representative because a considerable proportion of patients with acute aortic dissection die prior to admission, and data on prehospital deaths are not available [5].

Therefore, the putative association of pregnancy and acute dissection may, largely, be an artifact of selective reporting [13,14]. Population-based studies, such as the present one, may decrease these biases and provide a comprehensive epidemiologic insight.

2. Methods

This study was conducted in Vienna, the capital city of Austria in Europe, and comprises a fairly stable average population of 1 558 474 in the time frame of 1 January 1994 to 31 December 2004.

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This longitudinal study included both hospitalized and the non-hospitalized cases with acute type A aortic dissection within the female population in the age range of 15—45 years identified during the specified time interval.

All patients who required acute surgical intervention were identified at two tertiary care centers: at the Department of Cardiothoracic Surgery, Medical University of Vienna and at the Department of Cardiovascular Surgery, Lainz Hospital. All prehospital and in-hospital deaths occurring prior to definite diagnosis of acute aortic dissection were identified during autopsy at the Department of Forensic Medicine, Medical University of Vienna.

Acute aortic dissection was classified in accordance with the guidelines published by the European Society of Cardiology [15]. Patient data were collected on standardized forms that included information on patient demographics, history and clinical presentation, imaging findings, management, histopathological findings, and clinical events, including mortality. Completed data forms were forwarded to the Department of Emergency Medicine, Medical University of Vienna, which served as the coordinating center, and entered into an access database.

Basic demographic information, during the observation period, on the Viennese female population was provided by the Austrian Central Statistical Office (Österreichisches Statistisches Zentralamt; http://www.statistik.at). Further, in an attempt to estimate the incidence of acute aortic dissection during pregnancy, these authors used data from the Viennese live-birth and stillbirth database, which contains information on all births in Vienna. The information in this database has been collated from birth certificates and registrations of stillbirths.

The protocol for this study was approved by the respective institutional review boards for research at all study sites.

3. Statistics

Normally distributed continuous data are presented as the mean and the standard deviation, and non-normal distributed continuous data as the median and the interquartile range. Categorical variables are presented as absolute and relative frequencies. Comparative analyses of continuous data were performed by Mann—Whitney *U* tests, and groups of categorical data were compared by Fisher tests. To estimate the correlation between pregnancy and aortic dissection, the relative risks (RRs) and their respective 95% confidence intervals (CIs) were calculated. A two-sided *P*-value less than 0.05 was considered to be statistically significant. All calculations were performed with the Statistical Package for Social Sciences (SPSS) for Windows (version 10.0).

4. Results

4.1. Incidence

This study included subjects from the female population of Vienna, with an average 341 381 women in the age range of 15—45 years, who were followed up for 10 years (total of 3755.195 person-years of observation).

Overall, 15 patients (mean age: 38.8, SD: 4.8) with acute aortic dissection were included in this study, and indicate an overall incidence of 0.4 case per 100 000 person-years within the female population aged between 15 and 45 years.

Two cases of acute aortic dissection during late pregnancy were noted, and these indicated an incidence of 0.05 case per person-year. Calculating a total of 176 780 live- and stillbirths for the years of observation, an incidence of 1.1/100 000 live- and stillbirths/year was obtained.

4.2. Clinical and pathologic aspects

Arterial hypertension (93%), sudden onset of severe chest pain (73%), and neurologic symptoms, such as syncope (40%), were the leading symptoms of acute aortic dissection. The multi-slice thoracic computed tomography was the method of choice for confirmation of diagnosis (71%; Fig. 1). Idiopathic cystic medial necrosis and premature atherosclerotic disease were identified as the underlying aortic tissue pathology in the majority of patients (53%). A congenital predisposition was present in seven patients: hereditary connective tissue disease (Marfan and Ehler—Danlos syndromes) was present in four women, whereas congenital bicuspid aortic-valve disease was evident in one woman. Coarctation of aorta, corrected in early childhood, was identified as a risk factor in two other women. In the majority of patients, acute aortic dissection was the primary qualifying event for diagnosis of the underlying causative pathology. Pregnancy and aortic dissection were non-related events (RR: 3.27; 95%CI: 0.82—12.95; $P = 0.14$). Details of clinical data presented as pathologic aspects in these patients are depicted in Table 1.

Fig. 1. MRI in diagnosis of acute aortic dissection in a pregnant female in the 36th week of gestation. Syncope was the leading symptom on admission to the emergency department. Images were acquired on a Siemens Gyroscan Intera 1.5 T (bold arrow — dissection membrane in the ascending aorta; arrow — gravid uterus).

Table 1. Demographics, symptoms and underlying pathology of female patients under 45 years of age, suffering from acute aortic dissection. Assessment was performed via patient's, relative's interview and distinct medical chart review, as appropriate. Arterial hypertension was assumed in patients with documented history of hypertension or that with chronic intake of antihypertensive drugs. SCD: sudden cardiac death.

Patient (nr.)	Age (a)	Initial symptoms			SCD	Risk factors and aortic pathology					Preknown	Pregnancy (w)
		Chest pain	Syncope	Dyspnea		Hypertension	Marfan	Aortic coarctation	Cystic medial necrosis	Bicuspid aortic valve		
1	36	+	+	—	+	—	—	—	+	—	—	—
2	45	+	—	—	+	+	—	—	+	—	—	—
3	29	—	—	+	—	+	+	—	—	—	+	—
4	37	+	—	+	—	+	+	—	—	—	—	—
5	45	—	—	+	+	+	—	—	+	—	—	—
6	40	+	—	—	—	+	—	—	+	—	—	—
7	39	—	+	—	+	+	—	—	+	—	—	—
8	42	+	—	—	—	+	—	—	+	—	—	—
9	41	+	+	—	+	+	+	—	—	—	+	—
10	32	+	+	—	—	+	+	—	—	—	—	36
11	38	+	—	—	+	+	—	+	—	—	+	—
12	42	+	—	—	+	+	—	+	—	—	+	—
13	34	—	+	+	—	+	—	—	—	+	—	32
14	37	+	+	—	+	+	—	—	+	—	—	—
15	45	+	—	—	—	+	—	—	+	—	+	—
Cumulative count (%)		11 (73%)	6 (40%)	3 (20%)	8 (53%)	14 (93%)	4 (27%)	2 (13%)	8 (53%)	1 (7%)	5 (33%)	2 (13%)

4.3. Surgical management

In general anesthesia, cesarean section was initiated prior to emergency cardiac surgery in particular patients who were in the third trimester of pregnancy; however, definite surgical management of acute aortic dissection did not differ significantly from standard procedures. Details of surgical data are summarized in Table 2.

4.4. Mortality and outcome

Overall, on analysis, nine women died at the time of initial presentation (overall mortality: 60%): eight patients were identified with acute aortic dissection at forensic autopsy (prehospital mortality: 53%), and one woman had severe left ventricular failure and died during emergency surgery (in-hospital mortality: 6.6%). The follow-up of the other four patients (mean: 47 months) and the outcome in two pregnant patients and their offsprings were reported to be uneventful, with the exception of one mother who had Marfan's syndrome. The patient with Marfan's syndrome underwent successful cardiac transplantation 2 years later for severe myocardial infarction at initial presentation (see Table 3).

5. Discussion

This population-based study, for the first time, demonstrates that pregnancy may not be a risk factor for acute type A aortic dissection in women younger than 45 years of age. This life-threatening vascular emergency represents a rare pathology in women younger than 45 years of age; however, the condition is associated with a high rate of sudden death.

Information on the incidence of aortic dissection in the general population is limited. Previously reported studies have implied an incidence of 2.6—3.5 cases per 100 000 person-years [5]. Based on the results of this study, it is reported that this life-threatening pathology will occur in 0.4 case per 100 000 person-years within the female population in the age range of 15—45 years; this indicates that acute aortic disease may be primarily limited to advanced age [13].

The common, established risk factors for acute aortic dissection include hypertension, inherited disorders of connective tissue (Marfan's syndrome and Ehler—Danlos syndrome type IV), bicuspid aortic-valve disease, coarctation, aortitis, surgical manipulation, cardiac catheterization, and cocaine exposure [1]. Early studies based on autopsy reported that at least half of all aortic dissections reported in women younger than 40 years of age occur during pregnancy,

Table 2. Clinical characteristics and imaging modalities in patients admitted for emergency surgery of acute aortic dissection. Hemodynamic instability was defined as a permanent deterioration in systolic blood pressure below 90 mmHg at the Emergency Department and at the operating theatre and the need of preoperative advanced life support (ALS) including catecholamine support.

Patient (nr.)	Age (a)	Diagnostic imaging		Entry tear	Pericardial effusion	Hemodynamic stable
		CT	MRI	*Sinus valsalvae*		
3	29	—	+	—	—	+
4	37	+	—	+	—	+
6	40	+	—	+	—	+
8	42	+	—	+	+	—
10	32	+	—	+	—	+
13	34	—	+	+	—	—
15	45	+	—	—	—	+
Cumulative Count (%)		65 (71%)	2 (29%)	5 (71%)	1 (14%)	5 (71%)

Table 3. Surgical details and outcome data of female patients undergoing emergency surgical repair of acute aortic dissection. ECT: extracorporeal circulation time; HCA: hypothermic circulatory arrest; and RCP/ACP: retrograde/antegrade selective cerebral perfusion.

Patient (nr.)	Age (a)	ECT (min)	HCA (min)	Lowest esophageal temp (°C)	Selective cerebral perfusion	Composite graft	Hospital stay (d)	Follow-up (m)
3	29	219	30	14.8	RCP	+	26	97
4	37	203	36	16.2	RCP	—	12	90
6	40	233	30	16.1	RCP	+	8	40
8	42	—	35	15.5	ACP	—	—	—
10	32	240	23	16	ACP	—	9	41
13	34	220	—	16.3	—	+	14	10
15	45	228	20	15.7	ACP	—	12	4
Mean Count (SD)		224 (13)	29 (6)	15.8 (0.5)	6 (86%)	3 (43%)	13 (7)	47 (39)

most often in the third trimester or puerperium [3,6,7]. Pregnancy has, therefore, been reported to be an independent risk factor for aortic dissection within the female population [2,16].

The main predisposing factor for aortic dissection is the degeneration of collagen and elastin in the intima media of the aortic wall [1]. Systemic hypertension is considered the main risk factor in the average population. In the context of pregnancy and acute aortic dissection, estrogen has been identified to alter the structural integrity of the aorta, promote its remodeling and render it relatively more susceptible to injury during or shortly after pregnancy [17,18]. However, based on the observations in this study, pregnancy and aortic dissection are independent events: premature atherosclerosis and arterial hypertension, hereditary connective tissue disease, such as Marfan's and Ehler—Danlos syndromes, and previous aortic surgery or disease are the most common risk factors in aortic dissection occurring in women younger than 45 years. A continued predisposition, such as that constituted by the presence of Marfan's syndrome and bicuspid aortic-valve disease in two pregnant patients in the present study, may represent the main risk factor for aortic dissection in pregnancy. The speculation on hemodynamic stresses of pregnancy, labor, and parturition can contribute only secondarily and, therefore, does not explain the incidence of acute aortic dissection in pregnancy.

It may be concluded that the putative association of pregnancy and acute dissection may, therefore, largely be an artifact of selective reporting, which concurs with a review by Oskoui and Lindsay and results of a recent multi-center study [13,14]. This fact may be emphasized by the extensive literature available on management of aortic dissection in pregnancy, in spite of its low incidence [10,12,19,20]. Further, based on the observations in the present study, definite surgical management during pregnancy does not differ significantly from standard procedures. Immediate referral to surgery will result in the prognosis of favorable outcome for both mother and offspring.

The observed extensive prehospital mortality, however, cautions that, in women younger than 45 years of age, early diagnosis and treatment of hypertension may be an important strategy in the prevention of acute aortic dissection.

6. Limitations

Although this is the first population-based study to review the incidence, management, and outcome of acute aortic dissection in women younger than 45 years of age, certain minor limitations may apply: incidence may differ in other populations with different risk profiles and, therefore, the findings and conclusions of this study may not be completely generalizable. Residual confounding by patient-management in the emergency department, operating theater, and intensive care unit may be present. Such confounders are impossible to control in a population-based study and, rather, express the 'daily-life' characteristic of this study and provide external validity of the data obtained. Selection and information bias do not appear to be operative in this study, because the focus was on a clearly determined population where local laws demand an autopsy to detail and ascertain the cause of death in every case [21]. With the exclusion of these limitations, the conclusions of this study concur with that reported in previous reports.

7. Conclusion

The causal relationship between pregnancy and acute type A aortic dissection in women younger than 45 years of age is an artifact of selective reporting. Acute aortic dissection in pregnancy, a potentially lethal cardiovascular emergency, represents the primary qualifying event of an underlying causative pathology; therefore, screening for risk factors, at the least for hypertension, and definitive follow-up of patients who have undergone cardiac surgery in their childhood as a preventive measure appears mandatory within such a population. Despite extensive prehospital mortality, immediate referral to surgery, even during pregnancy, will result in a prognosis of favorable outcome.

Contributions

M. Thalmann: Data collection, final draft, and approval; G.H. Sodeck: Study design, coordination of study sites, data management, statistics, first draft, final draft, and approval; H. Domanovits: Study design, scientific and statistic advisory, study monitoring, final draft, and approval; M. Grassberger: Data collection, final draft, and approval; C. Loewe: Data collection, final draft, and approval; M. Grimm: Data collection, final draft, and approval; and M. Czerny: Data collection, scientific and statistic advisory, final draft, and approval.

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