SHORT- AND MEDIAN-TERM OUTCOME OF ACUTE STANFORD TYPE A AORTIC DISSECTIONS

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Contents

Summary

Background: Acute type A aortic dissections carry a high risk of serious complications and death. We here report the short- and median-term outcome for patients with this condition treated at the University Hospital of North Norway.

Material and methods: The records of all 43 patients (17 women) with acute type A aortic dissection admitted during 1998 – 2004 were analyzed.

Results: Mean age at onset was 61 (25 – 88) years. 33 (77 %) patients were treated with open surgery, and the most frequent procedure being resection and implantation of a tubular graft in the ascending aorta (58 %). Nine patients were deemed inoperable. In-hospital mortality was 35 % (95 % confidence limits (CL) 20-54) among the operated patients and 89 % (95 % CL 51-99) among those not operated. Predictors of in-hospital death were: no operation during index hospital stay (Odds ratio (OR) = 15, 95 % CL 2 – 132, P = 0,007), ECG changes at admission (OR = 10, 95 % CL 1 – 87, P = 0,027), age ≥ 70 years (OR = 5, 95 % CL 1 – 24, P = 0,02) and aortic cross clamp time > 122 minutes (OR = 9, 95 % CL 2 – 53, P = 0,009). The dominating causes of death were aortic rupture (30 %) and myocardial infarction (22 %). 25 % had aortic insufficiency and 15 % had neurological deficits at the last follow-up. 79 % of the follow-ups did not lead to any change in therapy.

Conclusions: In-hospital mortality at our institution is similar to that of the large International Registry of Acute Aortic Dissections (IRAD). Extended cross clamp times were associated with increased early mortality. We confirm the findings from IRAD that age ≥ 70 years and early ECG changes augment the risk of in-hospital death.

Introduction

Acute type A aortic dissection carries a high risk of serious complications and death (3). Much of the knowledge used to define treatment strategies is based on observational rather than randomized studies (4, 5). Treatment results vary a lot in different materials. For example, surgical mortality reported in different experiences from single centres or surgeons varies from 7 % to 30 % (5).

The most extensive observation study of aortic dissections is the International Registry of Acute Aortic Dissection (IRAD), which was established in 1996. 18 large referral centres in 6 countries contribute to the registry, which so far include 647 patients (31.12.01) with acute type A aortic dissection (5). Our hospital, The University Hospital of North Norway, has contributed data to the registry since 1998.

Mortality rate is high in the acute phase of type A dissections, 1% to 2 % per hour early after symptom onset (1). Modern surgical treatment improves the prognosis considerably. Some factors that predict high risk of in-hospital death have been identified (4). Among issues still controversial are the use of deep *versus* moderate hypothermia, whether to keep *versus* repair *versus* replace the aortic valve, the indications for aortic arch reconstruction and of selective cerebral circulation, the use of glue and the technique for distal anastomosis (open *versus* aortic cross clamping). Moreover, the recommended follow-up program (2) is neither based on hard evidence.

The aim of this study is to evaluate the outcomes for patients with acute type A aortic dissections treated in our hospital and compare these to multicenter experience. We also sought to identify risk factors for in-hospital death.

Material and methods

Patient selection

The University Hospital of North Norway (UNN) is a university hospital and it is the only cardiac surgical centre for a population of approximately 0,5 million people. In the period 01.01.98 – 31.12.04 43 patients with acute type A aortic dissection were treated in our hospital and all these are included in this study. Most patients were referred from local hospitals.

Data collection

For each patient up to 252 different variables were registered in a Microsoft Excel database which included demographics, known risk factors for dissection, course of the index hospital stay, treatment and outcome variables. The data collection was based on chart reviews and analysis of diagnostic imaging, including records from local hospitals where patients were followed up. For the patients who were still alive when the study was closed 31.12.04 the mean follow-up time was 1100 (82 – 2060) days.

Statistical analysis

Survival was analyzed with the SPSS 12.0 software for Windows using the Kaplan-Meier function. Predictors of in-hospital death were identified with Pearson`s Chi-Square test. Were expected count was less than 5 in one or more cells we used Fisher's exact test. Odds ratio for in-hospital mortality and major cardiovascular event was also computed in SPSS 12.0 for Windows.

Results

Study population

Patient characteristics are described in table 1. Among the 43 patients there was a small predominance of men (60 %). Mean age at debut was 61 years. One third of the patients were between 60 and 69 years. 7 % were less than 40 years. Among known risk factors for acute type A aortic dissection (1), the most frequent in our patient population was hypertension, which was present in 35 % of the patients. Median interval from onset of symptoms till first hospital admission was 2 hours and till diagnosis 13 hours.

Three patients were given a thrombolytic agent due to suspected acute myocardial infarction. Two of these patients died during the index hospital stay due to aortic rupture (death *in tabula*) and myocardial infarction.

Pathology

A majority of the patients (63 %) had a complete, classical dissection with distal extension to the abdominal aorta or beyond (table 2). In 46 % of the patients, one or more aortic branch arteries were involved in the dissection. Arch vessels were those most frequently involved.

Treatment

33 (77 %) of the 43 patients were treated with open surgery (table 3) and nine (21 %) were treated conservatively (not shown). One patient was treated with endovascular technique only, as the affection of the ascending aorta initially was overlooked. The most frequent reason for not operating was high patient age and/or co-morbidity (67 %). Other reasons were diagnostic delay (22 %) and small dissection (11 %).

The operative details for the 33 (77 %) patients primarily treated surgically are described in table 3. A majority of the patients were operated in deep hypothermia (88 %). The most frequent arterial cannulation site was femoral artery (61 %), while right atrium was the most frequently used venous cannulation site (73 %). In 79 % of the cases glue was used to fixate the disseceted layers distal to the distal anastomosis. 58 % received a tubular graft in the ascending aorta and 30 % received a composite graft. The majority was operated with an open distal anastomosis (78 %). 39 % had their aortic valve replaced.

Complications and use of resources during index hospital stay

Among the serious complications encountered during the index hospital stay were central nervous damage (26 %), myocardial infarction (21 %) and renal failure (19 %) (table 4). Ten patients (37 %) needed reoperation during the index hospitalization (table 4). A time interval from onset to diagnosis exceeding the median of 13 hours was associated with a higher incidence of a major in-hospital cardiovascular event (Odds ratio (OR) = 5, 95 % confidence limits (CL) 1 – 29), P = 0,047).

Mean duration of index hospital stay for the 43 patients were 27 (0-166) days. 28 of the patients needed intensive care during the index hospital stay and 27 needed mechanical ventilation (table 4). All surgical patients except one needed red blood cell transfusion. On average, they received 9 (1–23) units at the day of the operation and 14 (1-32) units during the entire hospital stay. Twenty-two patients received thrombocyte transfusions (1 – 5, on average 2 units during the entire hospital stay).

Outcome

In all, 47 % (95 % CL 31 – 62) died during index hospital stay. Among the patients who were not operated the in-hospital mortality was 89 % (95 % CL 51 – 99). In contrast, the in-hospital mortality among those operated was 35 % (95 % CL 20 – 54). With that, not being operated was associated with higher in-hospital mortality (OR = 15, 95 % CL 2 – 132, P = 0,007). The total mortality was 89 % among those not operated and 44 % among those operated (P = 0,0002). 15 patients died during the first 3 days after admission to hospital. Survival function is described in figure 1.

IRAD has described seven predictors of in-hospital death: Abrupt onset of pain, abnormal ECG, any pulse deficit, kidney failure and hypotension/schock/tamponade on presentation together with age ≥ 70 years and female gender (4). The risk factor distribution in our study population was very similar to that of the aggregated IRAD population (table 5) from which these risk factors and their relative weights were identified (4). Our data confirm age ≥ 70 years (OR = 5, 95 % CL 1 – 24, P = 0,02) and abnormal ECG (OR = 10, 95 % CL 1 – 87, P = 0,027) as predictors of in-hospital death. Moreover, aortic cross clamp time exceeding the median of 122 minutes was associated with a higher in-hospital mortality (OR = 9, 95 % CL 2 – 53, P = 0,009).

Aortic cross clamp time > 122 minutes was also associated with a major in-hospital cardiovascular event and/or in-hospital death (OR = 5, 95 % CL 1 – 23, P = 0,033).

Mortality

Of the 23 patients who died, eight (35 %) were not operated, six (26 %) died during the index operation, six (26 %) during the rest of the index hospital stay and three (13 %) post discharge (table 6). The most frequent cause of death was aortic rupture (31 %).

Course post discharge

Only a single patient underwent secondary surgery related to the dissection after discharge (table 7). The indication for surgery was identified outside regular follow-ups.

Blood pressure management is assumed to be important to prevent progression of the dissection, aneurismal aortic dilatation and other complications to the dissection (2). Ten (44 %) of our patients had blood pressure values within the recommended levels of < 135/80 mmHg (2) at every follow-up whereas four (17 %) had values outside the recommended levels at every follow-up (table 7).

Some patients had chronic disabilities after discharge from index hospital stay (table 7), and most frequent was aortic insufficiency (25 %). At the time of last follow-up three (15 %) patients had neurological deficits.

With minor modifications, we adhered to a consensus-based follow-up regimen (2). The 23

patients who survived beyond the index hospitalization had 98 follow-ups during the study period (table 8). 21 (21 %) of these follow-ups lead to change in medication, none lead to referral for surgery while a vast majority of 77 (79 %) of the visits did not lead to any change in therapy.

Discussion

Hypertension is one of the important known risk factors of aortic dissection (1). In the IRAD material 69 % of the patients with acute type A aortic dissection had a history of hypertension (4) while only 35 % of the patients in our material. 26 % of our patients had an intramural hematoma. In IRAD the proportion of patients with intramural hematoma was 8 % (4). 9 % of our patients had an iatrogenic dissection, as compared to 7 % of those in the aggregated IRAD population (4). The distribution of known risk factors of intrahospital death (4) was quite equal in our material and in IRAD. According to the formula of predicting in-hospital mortality published by Metha et al (4) and calculations done by Dean Smith in the IRAD-group the predicted in-hospital mortality for our mean patient was 33 % (assumed treatment quality in our hospital do not differ from the average of the IRAD-centres).

One of the important aims of this project was to compare in-hospital mortality in our hospital with the IRAD multicenter experience. The in-hospital mortality among our operated patients was 35 %, and the 95 % CL of 20 – 54 % encompasses the 27 % in-hospital mortality of the aggregated IRAD population (4). Thus, the quality of care offered by our institution seems not to differ from the average of the IRAD centres.

The portion of patients who were treated primarily surgically was similar in our material and in the aggregated IRAD population (4) (79 and 72 % respectively), as were the reasons for declining to operate. As expected (4), we found that surgical treatment itself is a powerful predictor of

survival the index hospitalization: odds ratio for death for operated *versus* not operated was 0,07 (95 % CL 0,008 – 0.6). This is in agreement with reports from IRAD (4).

We found that an extended aortic cross clamp time was a relatively strong predictor of death (OR = 9, 95 % CL 2 – 53, P = 0,009). One of the possible explanations is that the patients with extended aortic cross clamp time perhaps were those with the most extensive aortic pathology.

In contrast to the IRAD report (4), in which the cause of death was specified only for 2/3 of the patients, we have been able to identify the cause of death in all patients who died during the study period. The most frequent cause of death is, in present study as in the IRAD report aortic rupture (31 % in present study and 33 % in IRAD) (4). Myocardial infarction was one of the major causes of death in our material (22 %) while in IRAD, myocardial infarction was not reported as the cause of death for any of the patients (4).

IRAD has reported seven predictors of in-hospital death in patients with acute type A aortic dissection (4). Our study confirms two of these, i.e. predictors: age $\geq$ 70 years (P = 0,02) and abnormal ECG on presentation (P = 0,027). Surprisingly, we did not find any prognostic effect of circulatory collapse early after admission, which was a strong risk factor in the IRAD report (4). We suspect that this reflects a statistical coincidence in our relatively small patient sample.

It has been estimated that nearly one third of patients surviving initial treatment for acute type A aortic dissection will experience extension of their dissection or aortic rupture or will require surgery for aortic aneurysm formation within 5 years of presentation (2). It is therefore thought to be important to follow these patients, especially with hypertension treatment and repeated aortic

imaging (2). International recommendations suggest follow-up including image studies at 1, 3, 6, 9 and 12 months after discharge and annually thereafter (2). We have studied follow-ups of the patients the first 3-4 years after onset of dissection. Notably, only 21 % of the follow-up visits lead to any change in therapy, and in all those cases adjustments of antihypertensive medication was the only therapeutic consequence. None of the follow-ups lead to referral to surgery. These findings seem to indicate that a general practitioner could manage follow-up of a large proportion of these patients, at least the first years. Our data suggest that the use of imaging studies could be considerably reduced compared to the recommendations and frequent imaging studies should probably be used more selectively, for example for those with known aortic insufficiency (eccocardiography) and those with a considerable aortic dilation (computed tomography or magnetic resonance).

Conclusions

In-hospital mortality at our institution is similar to that of the large International Registry of Acute Aortic Dissections (IRAD). As in IRAD our study shows a significant higher survival in patients who were treated with surgery *versus* conservative treatment. The present study confirms age and ECG-findings as prognostic factors. We identify aortic cross clamp time as a prognostic factor. Our study indicates that a general practitioner could manage follow-up of a large proportion of these patients, at least the first few years, and that the use of image studies could be reduced and more selectively used.

Table 1 Characteristics of 43 patients with acute type A aortic dissection admitted between 1998 and 2004

Category	
Mean age (years) (range)	61 (25 - 88)
	n (%)
Gender	
Male	26 (60)
Female	17 (40)
Risk factors and comorbidities	
Hypertension	15 (35)
Genetic syndrome*	1 (2)
Known aortic aneurysm	5 (12)
Bicuspid aortic valve	3 (7)
Aortic valve vitium	5 (12)
Diabetes mellitus	1 (2)
Pregnancy	1 (2)
Iatrogenic dissection	4 (9)
Previous invasive cardiac procedures	
Open heart surgery	6 (14)
Catheterization and/or PCI	4 (9)
Thrombolytic agent administered in the course of index dissection**	3 (7)
Time course (h) (median (range))	
Interval from onset till first hospital admission***	2 (0 - 168)
Interval from onset till diagnosis****	13 (2 - 216)

*One patient had Turner syndrome, none had other known genetic syndromes known to predispose aortic dissection

**Invariably due to suspected acute myocardial infarction.

***Data missing for 17 patients. 13 of those had time to admission less than 24 hours and 2 less than 2 hours.

***Data missing for 17 patients. 12 of those had time to diagnosis less than 24 hours and 1 less than 4 hours

Table 2 Aortic pathology in 43 patients with acute type A aortic dissection

Category	n (%)
Type of dissection	
Classical dissection	32 (74)
Intramural hematoma	11 (26)
Distal extension of the dissection*	
Ascending aorta	4 (9)
Aortic arch	8 (19)
Descending aorta	2 (5)
Abdominal aorta or beyond	27 (63)
Aortic branch arteries involved**	
Brachiocephalic trunk, carotid and/or subclavian artery	17 (40)
Coeliac trunk	2 (5)
Superior mesenteric artery	2 (5)
One renal artery	10 (23)
Left	7 (16)
Right	3 (7)
Both renal arteries	1 (2)
None	19 (44)

*Data missing for 2 patients

**Data missing for 3 patients

Table 3 Operative details for those 33 patients out of 43 with acute type A aortic dissection who were treated surgically

Operation variables	
Time intervals (mean (range))	**Duration (min)**
Entire procedure	329 (210 - 480)
Extracorporeal circulation	209 (102 - 394)
Aortic cross clamping (n = 32)*	117 (54 - 236)
Circulatory arrest (n = 28)	30 (5 - 60)
	n (%)
Deliberate interruption of systemic perfusion	
Circulatory arrest	28 (85)
None	5 (15)
Selective cerebral circulation**	12 (36)
Hypothermia	
Moderate	4 (12)
Deep	29 (88)
Primary arterial cannulation site	
Right subclavian artery	11 (33)
Aortic arch	1 (3)
Femoral artery	20 (61)
More than one cannulation site	1 (3)
Subsequent cannulation of aortic prosthesis	13 (39)
Venous cannulation site	
Right atrium	24 (73)
Femoral vein	5 (15)
Both right atrium and femoral vein	4 (12)
Application of glue between dissection layers	
In ascending aorta	20 (61)
In aortic arch	13 (39)
Graft	
Tubular graft in ascending aorta	19 (58)
Composite prosthetic aortic valve + tubular graft in ascending aorta	10 (30)
Composite prosthetic aortic valve + tubular graft in ascending aorta and aortic arch	3 (9)
None***	1 (3)
Technique for distal anastomosis (n=32)****	
Open	25 (78)
With aortic cross clamp	7 (22)
Aortic valve procedure	
Reconstruction	3 (9)
Replacement	13 (39)
Bioprosthesis	2 (15)
Mechanic prosthesis	11 (85)
None	17 (52)
Arch reconstruction	
Partial	4 (12)
Total	4 (12)
Simultaneous coronary artery bypass grafting	7 (21)
Other concomitant procedures*****	5 (15)

*1 patient was operated without aortic cross clamping.

**All 12 patients were operated with circulatory arrest and with open distal anastomosis. All except 1 patient were operated in deep hypothermia.

***This was a patient with a minor, iatrogenic dissection

****1 patient had no graft constructed, therefore n=32

*****These procedures were femofemoral crossover, secondary correction of ventricular septal defect, reconstruction/strengthening of ruptured infarction lower wall of the heart and admission of intra aortic balloon pump, vein plastic on the right axillary vein and admission of aortic balloon pump.

Table 4 Course of index hospital stay for 43 patients with acute type A aortic dissection

Variable	
Duration of hospital care (days) (mean (range))	
Index hospital stay	27 (0-166)
Intensive care (n=28)	7 (1-25)
Mechanical ventilation (n=27)	7 (1-22)
	n (%)
Complications	
Central nervous damage*	11 (26)
Myocardial infarction	9 (21)
Renal failure necessitating substitution treatment	8 (19)
Neurological deficits at the time of discharge (n=23)**	5 (22)
Patients with secondary open surgery (n=27 survivors of primary operation)	10 (37)
Reoperation because of bleeding	3 (30)
Reoperation because of cardiac tamponade	2 (20)
Leg fasciotomy	2 (20)
Pacemaker implantation	1 (10)
Diagnostic laparoscopy because of intestinal malperfusion	1 (10)
Anastomosis leakage and femur amputation	1 (10)
Outcome	
In-hospital mortality	20 (47)
Death *in tabula*	6 (14)
Discharged to home	22 (51)
Discharged to nursing home	1 (2)

*Type of central nervous damage (number of patients): Cerebrovaskular accident/ stroke (5), brain damage because of hypoksemia (3), spinal ischemia (1) and cerebral dysfunction (1).

**Type of neurological deficits: reduced cognetive function, lightly redused strength right arm, redused strength/paralysis right leg and recurrence paresis/hoarseness, unsteadiness and redused vision, difficulties in reading.

Table 5 Distribution of risk factors for intra-hospital death in the present study (n=43) vs. that of the International Registry of Acute Aortic Dissections (IRAD) (n=547)

Risk factor	**Present study**	**IRAD (4)**
	n (%)	**n (%)**
Age > 70 years	11 (26)	192 (35)
Female	17 (40)	190 (35)
Abrupt onset pain on presentation*	36 (84)	435 (85)
Abnormal EKG on presentation**	31 (72)	391 (70)
Any pulse deficit on presentation***	8 (19)	153 (30)
Kidney failure on presentation and before surgery****	6 (14)	28 (6)
Hypotension/shock/tamponade on presentation	12 (28)	154 (29)

*Data missing for 2 patients

**Data missing for 3 patients

***Data missing for 3 patients

****Data missing for 1 patient

Table 6 Cause and time of death in patients with acute type A aortic dissection (n=23)

	n (%)	Time (days) (mean (range))*
Managed conservatively	**8 (35)**	**3 (1-13)**
Aortic rupture without cardiac tamponade	1 (4)	1 (1-1)
Cardiac tamponade	1 (4)	1 (1-1)
Myocardial infarction	2 (9)	1 (1-1)
Stroke	1 (4)	2 (2-2)
Visceral ischemia	1 (4)	3 (3-3)
Multi-organ failure	1 (4)	13 (13-13)
Operated	**15 (65)**	**76 (1-712)**
In tabula	6 (26)	3 (1-9)
Aortic rupture without cardiac tamponade	4 (17)	4 (1-9)
Myocardial infarction	2 (9)	2 (1-2)
In-hospital, postoperatively	6 (26)	19 (2-100)
Aortic rupture without cardiac tamponade	1 (4)	4 (4-4)
Myocardial infarction	1 (4)	5 (5-5)
Pulmonary embolism	1 (4)	100 (100-100)
Visceral ischemia	1 (4)	3 (3-3)
Multi-organ failure	2 (9)	2 (2-2)
Post discharge	3 (13)	334 (24-712)
Aortic rupture without cardiac tamponade	1 (4)	24 (24-24)
Visceral ischemia	1 (4)	265 (265-265)
Pneumonia	1 (4)	712 (712-712)

*Time from first hospitalization to death

Table 7 Course post discharge for 23 patients with acute type A aortic dissection

Category	n (%)
Readmissions due to suspected complication to aortic dissection	7 (30)
Effectiveness of blood pressure management*	
Patients within recommended BP levels at every follow-up	10 (44)
Patients within recommended BP levels at some follow-ups	7 (30)
Patient outside recommended BP levels at every follow-up	4 (17)
Patients with secondary dissection-related surgery post discharge	
Open surgery**	1 (4)
Interventional radiology	0 (0)
Chronic disabilities	
Dialysis after discharge	0 (0)
Neurological deficits at the time of last follow-up (n=20)	3 (15)
Intermittent claudication at the time of last follow-up (n=20)***	0 (0)
Aortic insufficiency (> grade 2) at the time of last follow-up (n=20)****	5 (25)
Institutionalised in nursing home*****	1 (4)
Progress of dissection from time of diagnosis to last control (n=20)******	2 (10)

*The recommendations are systolic and diastolic pressures below 135 and 80 mmHg, respectively.[2] Data were missing for 2 patients.

**The patient had a deep sternal wound infection and underwent 15 revisions.

***Data missing for 1 patient

****Data missing for 5 patients

*****Data missing for 1 patient

******Data missing for 1 patient.

Table 8 Role of regular out-patient clinic controls in follow-up decision-making for 23 patients with acute type A aortic dissection

Therapeutic consequence of out-patient visits	**n* (%)**
No change in therapy	77 (79)
Change in medication	21 (21)
Referral to surgery	0 (0)

*n = number of visits

Figure 1 Kaplan-Meier survival function

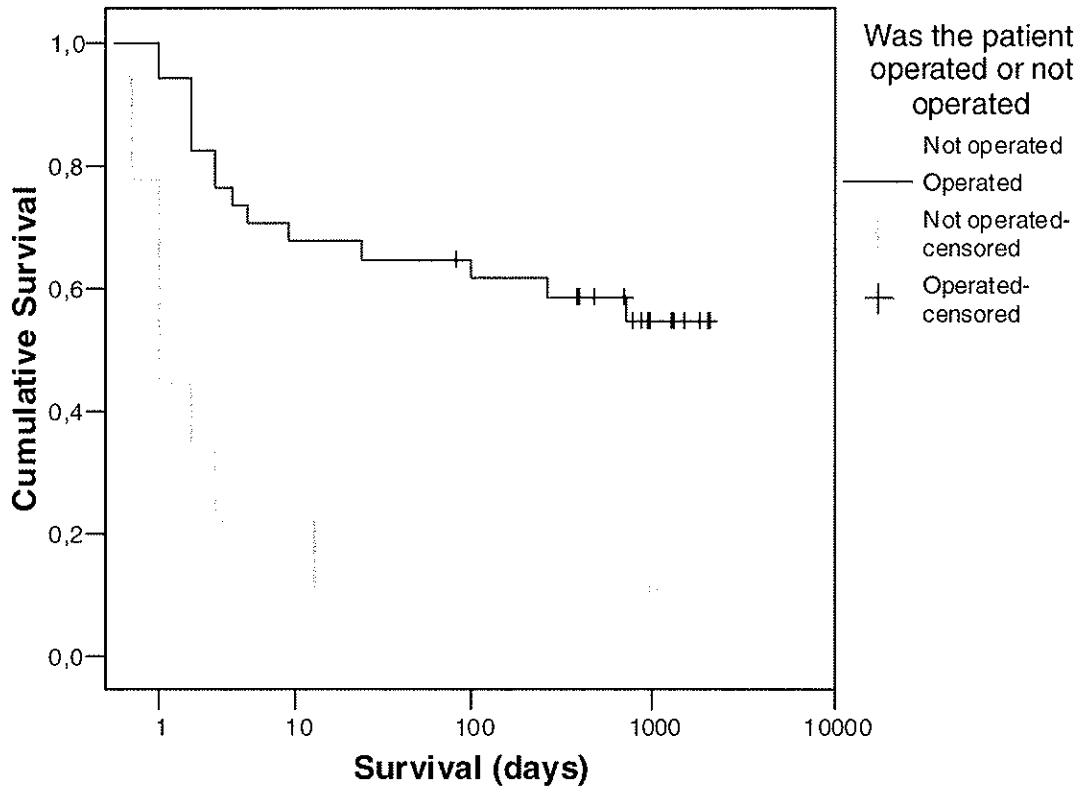

Figure 1: The figure shows survival function separately for operated and not operated patients. On the x-axis is survival in days and on y-axis cumulative survival. All censored patients are market on the curve.

References

1. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management. Part I: From etiology to diagnostic strategies. *Circulation.* 2003;108:628-635.
2. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management. Part II: Therapeutic management and follow-up. *Circulation.* 2003;108:772-778.
3. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, Evangelista A, Fattori R, Suzuki T, Oh JK, Moore AG, Malouf JF, Pape LA, Gaca C, Sechtem U, Lenferink S, Deutsch HJ, Diedrichs H, Robles JM, Llovet A, Gilon D, Das SK, Armstrong WF, Deeb GM, Eagle KA. The International registry of acute aortic dissection IRAD. New insights into an old disease. *JAMA.* 2000;283:897-903.
4. Mehta RH, Suzuki T, Hagan PG, Bossone E, Gilon D, Llovet A, Maroto LC, Cooper JV, Smith DE, Armstrong WF, Nienaber CA, Eagle KA. Predicting death in patients with acute type A aortic dissection. *Circulation.* 2002;105:200-206.
5. Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Mehta RH, Bossone E, Cooper JV, Smith DE, Menicanti L, Frigiola A, Oh JK, Deeb MG, Isselbacher EM, Eagle KA. Contemporary results of surgery in acute type A aortic dissection: The International Registry of Acute Aortic Dissection experience. *The Journal of Thoracic and Cardiovascular Surgery.* 2005;129:112-22