Impact of donor-transmitted coronary atherosclerosis on quality of life (QOL) and quality-adjusted life years (QALY) after heart transplantation

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Abstract

Background: In 5-10% of HTX significant coronary artery sclerosis is transmitted. This study evaluates the impact of donor-transmitted coronary artery sclerosis (DCAS) on quality of life (QOL) and quality-adjusted life years (QALY) after transplantation.

Methods: In 1253 consecutive transplantations single-vessel DCAS was found in 53 patients (DCAS1 group) and double- or triple-vessel DCAS in 26 patients (DCAS2/3 group). Health-related QOL was analyzed by the "Short-Term Inventory 36 Health Survey" (SF-36) scale and QALY were calculated. Patients without DCAS, who were matched for sex, age, indication and time after transplantation, served as controls (NDCAS).

Results: Thirty-day mortality in groups NDCAS, DCAS1 and DCAS2/3 was 12.2%, 13.2% and 61.5%, respectively. However, beyond the first year the annual decrease in all groups was comparable (5.4%/year, 4.3%/year, and 5.0%/year). The SF-36 questionnaire showed no significant differences between the groups in the long-term survival. Quality-adjusted life years were comparable in groups NDCAS (8.0 QALY) and DCAS1 (8.5 QALY) but worse in DCAS2/3 (2.2 QALY).

Conclusions: DCAS represents a risk for early graft failure but impairs neither long-term survival thereafter nor quality of life (QOL). Donor screening by angiography seems to be a good investment to avoid the loss of about 6 quality-adjusted life years (QALY) by transmitted coronary atherosclerosis.

Key words: coronary atherosclerosis, heart donor, quality of life, quality adjusted life years, QALY, heart transplantation

Introduction

Within the past 20 years and for different reasons, a clear change in the profile of the typical heart donor has come about. About 25% of donors in Europe are older than 50 years and the most frequent cause of brain death is no longer a cerebral trauma but spontaneous intracranial bleeding (1). Thus, today the donor pool does not represent a young and healthy population, but a population in middle age with an elevated cardiovascular risk profile and a prevalence of significant coronary artery sclerosis in the donor pool of

about 20% (2). Regardless of this development donor hearts are unfortunately still regarded as if they were young, healthy organs; how otherwise is it to be explained that in Europe coronary angiography is performed in only about 5% of the heart donors (3)?

Since this deplorable situation cannot be changed at least in the short term, one has to assume that 5-10% of the transplants will continue to transfer significant coronary atherosclerotic lesions unintentionally, whereby the risk for early graft failure is significantly increased (2, 4). On the other hand, it has been shown that patients who survived the direct post-operative phase after implantation of a coronary atherosclerotic donor heart have a further life expectancy that is comparable to that of recipients of healthy grafts (2).

Therefore, the purpose of this study was to evaluate the impact of donor-transmitted coronary artery sclerosis (DCAS) on quality of life (QOL) and quality-adjusted life years (QALY) after transplantation.

Patients and methods

Patients

A total of 1253 consecutive HTx recipients were investigated retrospectively for donor-transmitted coronary atherosclerosis (DCAS) (2). Donor-transmitted coronary atherosclerosis was defined as focal atherosclerosis with stenosis of at least 50%. Eighty-five out of 1253 (6.8%) cases were excluded, since coronary evaluation was not performed within 6 months (n=45) or hearts had undergone pre-transplant angiography (n=40).

In 1086 patients no donor-transmitted coronary atherosclerosis was found (NDCAS group) and in 82 patients (7%) donor-transmitted coronary atherosclerosis was diagnosed by angiography (n=49) or autopsy (n=33). Single-vessel donor-transmitted coronary atherosclerosis was found in 53/82 patients (DCAS1 group) and double- or triple-vessel donor-transmitted coronary atherosclerosis in 26/82 patients (DCAS2/3 group). In
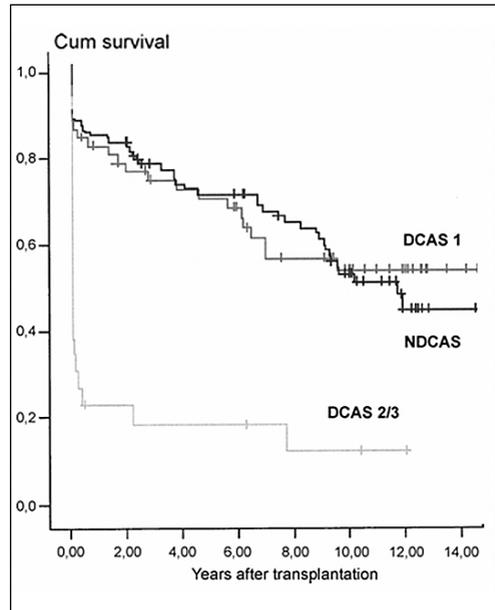

Figure 1: Cumulative survival after transplantation of donor hearts with donor-transmitted coronary atherosclerosis in a single vessel (DCAS1), of donor hearts with diffuse donor-transmitted coronary atherosclerosis (DCAS2/3) and healthy donor hearts (NDCAS) (reprinted from 2 by permission of the publisher).

three of the 82 patients, donor-transmitted coronary atherosclerosis was found but the autopsy report was unclear regarding the degree of atherosclerosis.

Thirty day post-HTX cumulative survival in groups NDCAS, DCAS1 and DCAS2/3 was 87.8%, 86.8% and 38.5%, respectively (Fig. 1). However, beyond the first year the annual decrease in all groups was comparable (5.4%/year, 4.3%/year, and 5.0%/year).

Methods

Health-related quality of life analysis
The Medical Outcomes Trust (MOT) "Short-Term Inventory 36 Health Survey" (SF-36) scale was used to analyze the heart transplant patients' health-related quality of life (QoL) (5). The SF-36 scale contained 36 ques-

tions in 8 different subscales designed to assess physical and mental health.

All 29 patients in the groups DCAS1 (n=21) and DCAS2/3 (n=8) who were still alive were enrolled in the health-related quality of life analysis. Thirty-six patients from the group NDCAS, who were matched for sex, age, indication and length of post-transplant period, served as the control group (DCAS control).

Quality-adjusted life years (QALY)

Quality-adjusted life years (QALY) are the arithmetic product of "lived life-years" or "life expectancy" and a measure of the quality of the remaining life-years (6). "Lived life-years" of our transplant patients were computed by planimetry of the area under the curve of the corresponding cumulative survival curves, which were extrapolated for a period of 30 years. Extrapolation was performed assuming that the annual decrease observed beyond the first year after transplantation was constant in each group (5.4%/year in group NDCAS, 4.3%/year in group DCAS1 and 5.0%/year in group DCAS2/3) (Fig. 2).

The mean value of the 8 different subscales of the SF-36 analysis is used as the measure of quality of life during this period, i.e. "remaining life-years" or "lived life-years".

Coronary vessels were screened by angiography for macrovasculopathy.

Statistical analysis was performed using Kaplan-Meier analysis and the log-rank test.

Results

Health-related quality of life analysis

In none of the 8 different subscales of the SF-36 analysis were significant differences between groups (DCAS1, DCAS2/3 and DCAS control) found, i.e. in the long-term, survival and physical and mental health-related quality of life (QoL) of the transplant recipient is not impaired by coronary atherosclerosis of the donor graft (Table 1).

This seems to be true even if more than a single coronary is involved (group DCAS2/3) and despite the fact that more coronary interventions were performed in the DCAS groups than in the NDCAS group (Table 2).
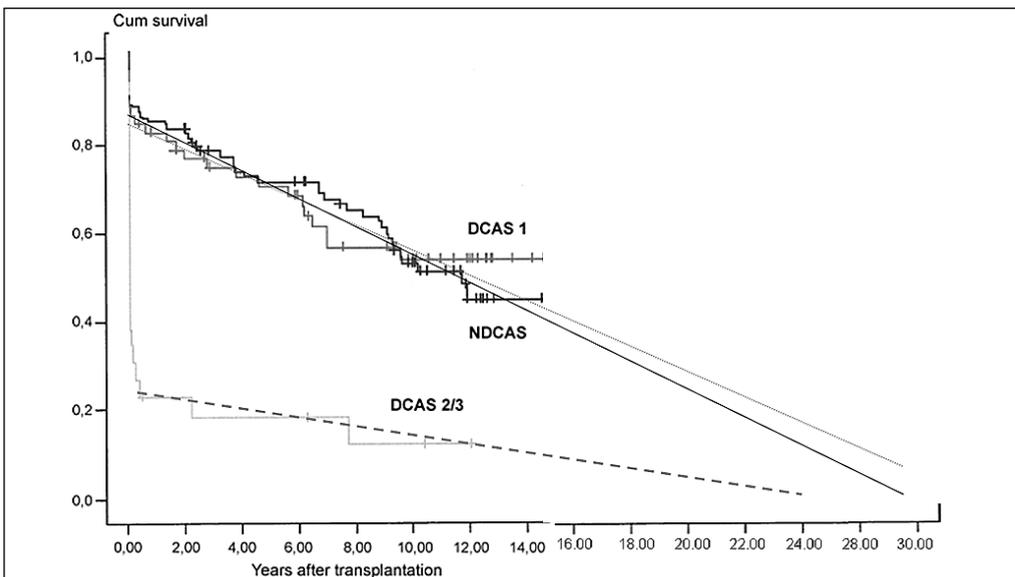

Figure 2: Extrapolation of cumulative survival curves for groups DCAS1, DCAS2/3 and ND-CAS for 30 years.

Table 1: Group statistics of Short-Term Inventory 36 (SF-36) scale.

	Group	Mean	Std. Deviation	Std. Error Mean	P-values
Role Physical Scale	DCAS1	70.5	38.34	9.90	0.51 / 0.45 → 0.26
	DCAS2/3	64.9	39.64	12.21	
	Control	65.1	43.61	4.40	
Bodily Pain Scale	DCAS1	54.3	31.44	7.86	0.27 / 0.34 → 0.37
	DCAS2/3	58.9	32.02	7.01	
	Control	57.4	34.08	3.39	
Physical Functioning Scale	DCAS1	58.9	27.92	6.98	0.17 / 0.44 → 0.34
	DCAS2/3	55.1	28.37	6.42	
	Control	64.0	26.05	2.54	
General Health Scale	DCAS1	58.2	20.51	5.12	0.63 / 0.45 → 0.33
	DCAS2/3	61.3	30.27	5.24	
	Control	52.3	15.41	1.51	
Vitality Scale	DCAS1	60.6	11.93	2.98	0.23 / 0.39 → 0.42
	DCAS2/3	58.1	12.04	3.04	
	Control	53.8	19.95	1.96	
Social Functioning Scale	DCAS1	71.7	21.39	5.34	0.45 / 0.27 → 0.38
	DCAS2/3	69.1	24.20	6.21	
	Control	75.3	23.35	2.27	
Role Emotional Scale	DCAS1	90.2	21.11	5.64	0.31 / 0.44 → 0.39
	DCAS2/3	75.4	24.23	3.72	
	Control	76.4	38.01	3.86	
Mental Health Scale	DCAS1	52.5	11.47	2.86	0.41 / 0.54 → 0.38
	DCAS2/3	49.2	10.29	3.42	
	Control	54.9	17.47	1.72	
Mean values of all 8 subscales	**DCAS1**	**64.6**			
	DCAS2/3	**61,5**			
	Control	**62.4**			

Table 2: Number of coronary angiographies and coronary interventions (PTCA/stent) in absolute numbers and per patient during the first post-HTX year. Left ventricular function (LV-EF) at first coronary angiography post HTX (angio) and in echocardiography at time of SF36-evaluation (echo).

| | # of coronary angiographies during 1st year | # of coronary interventions during 1st year | LV-EF (angio) | LV-EF (echo) |
	absolute / per pat.	absolute / per pat.		
DCAS1 (n=53)	82 / 1.5	24 / 0.5	65% (± 11%)	55% (±12%)
DCAS2/3 (n=26)	34 / 1.3	22 / 0.8	58% (±8%)	59% (±10%)
NDCAS (n=1086)	1114 / 1.0	0 / 0	62% (±10%)	58% (±7%)

*Table 3: Lived life-years are computed by planimetry, i.e. area under the curve of the corresponding survival curve. *Lived life-years were computed in all NDCAS patients (n=1086). ** Health-related quality of life is determined by SF-36 questionnaires in the control group, i.e. only 36 out of 1086 NDCAS patients (see methods section).*

	Lived life-years	Health related QoL	QALY
NDCAS/Control	12.9*	62.4 %**	8.0
DCAS1	13.1	64.6%	8.5
DCAS2/3	3.5	61.5 %	2.2

Quality-adjusted life years (QALY)

Quality-adjusted life years were comparable in groups NDCAS (8.0 QALY) and DCAS1 (8.5 QALY) but worse in DCAS2/3 (2.2 QALY) (Table 3; Fig. 3a-c).

No differences between the groups were found in the de novo development of post-transplant macrovasculopathy.

Discussion

During the past two decades the mean age and the cardiovascular risk factor profile of heart donors have increased worldwide (1, 7). Despite the high prevalence of coronary atherosclerosis in the donor pool, screening angiography is performed rarely (3). It has been shown that this inadequate donor management results in donor-transmitted coronary atherosclerosis in a considerable number of cases and that those grafts are more likely to develop early graft failure after cardiac transplantation (2, 4, 8).

On the other hand, it has been found that, in patients who survive implantation of coronary-diseased organs in the short term, further survival is comparable to survival of recipients of healthy grafts, i.e. long-term survival beyond the first year seems to be independent of the degree of coronary involvement (2). However, this raises the question of whether quality of life may be impaired and the costs involved higher if donor coronary atherosclerosis is transmitted.
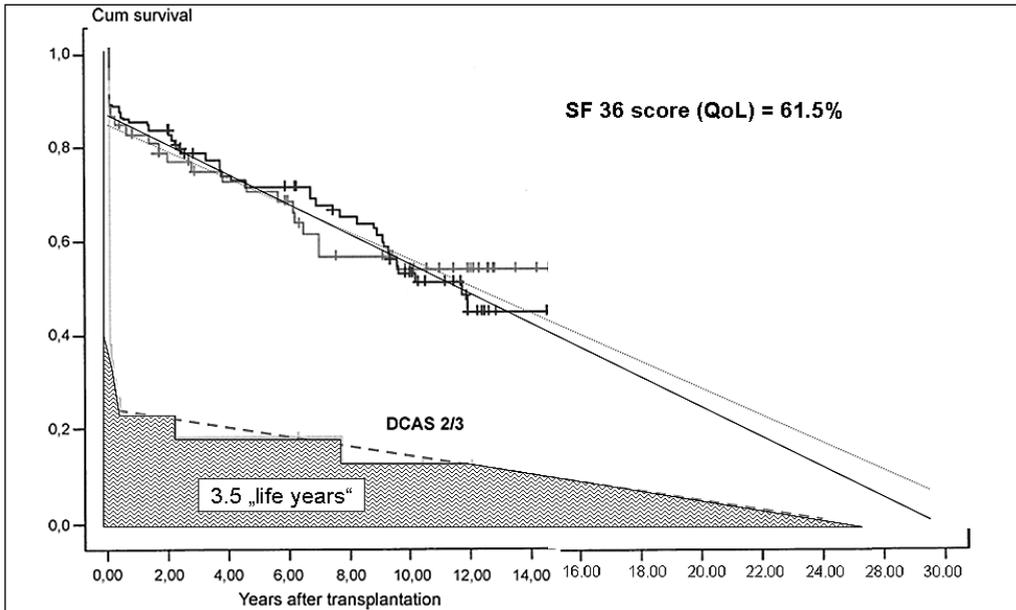
Figure 3a: "Life-years" (or "life expectancy") in group DCAS2/3, computed by planimetry of the area under the curve of the corresponding cumulative survival curve. SF 36 score = mean value of 8 different subscales of health-related quality of life analysis in group DCAS2/3, i.e. a measure of quality of life (QoL) during "life-years".
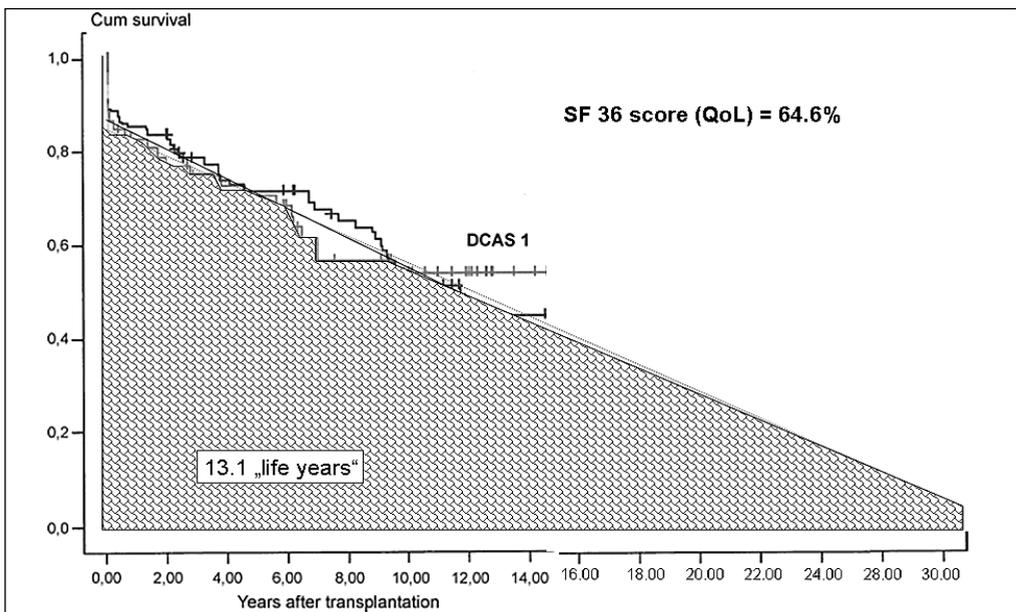

Figure 3b: "Life-years" (or "life expectancy") in group DCAS1, computed by planimetry of the area under the curve of the corresponding cumulative survival curve. SF 36 score = mean value of 8 different subscales of health-related quality of life analysis in group DCAS1, i.e. a measure of quality of life (QoL) during "life-years".

Health-related quality of life

Heart transplantation improves health-related quality of life (HRQOL) patients considerably in comparison with their pre-transplant situation and this continues for many years; however, norm-based comparisons suggested lower health-related quality of life for all dimensions except mental health (5, 9). Health-related quality of life found in our patients after heart transplantation corresponded to the findings in other programs (5, 9).

Surprisingly, health-related quality of life seems not to be impaired by coronary atherosclerotic lesions transmitted by means of transplantation (Table 1). On the other hand, at least in the survivors investigated, myocardial function was not impaired by transmitted coronary disease and, due to surgical denervation during the transplant procedure, any potentially existing myocardial ischemia would not cause angina. Furthermore, one has to consider that with regard to the clinical impact of transmitted coronary lesions the survivors investigated presumably represent a highly selected subgroup. Whether the other grafts would also offer good health-related quality of life if the early post-transplant outcome could have been improved by complete revascularization during transplantation – assuming that myocardial performance had been normal – is a question that has to remain unanswered so far. Successful heart transplantations with concomitant CABG even in multi-vessel diseased donor organs have been reported by different centers, but only in very few patients and evaluation of health-related quality of life in those recipients is not provided (10, 11, 12, 13).

Also the number of coronary angiographies per patient in groups DCAS1 and DCAS2/3 was not much higher than in group NDCAS, since all patients have to undergo this investigation according to the post transplant guidelines of our program (Table 2). However, there were more coronary interventions (PTCA, stent) in groups DCAS1 and DCAS 2/3, but the additional burden of PTCA and/or stent implantation in comparison to a simple angiography without intervention seems not to impair health-related quality of life significantly.

Quality-adjusted life years

The quality-adjusted life year (QALY) is a measure that includes both the quality and the quantity of life lived after an intervention. Thus it makes the impact of health interventions measurable as well as making two or more health interventions comparable (6). By calculation of "costs per gained QALY" the concept can also be used in a cost-utility analysis.

The fact that QALY in group DCAS2/3 is only 2.2 compared to 8.0 and 8.5 QALYs in the groups NDCAS and DCAS1, respectively, means that transplantation of diffuse atherosclerotic grafts is about 4-fold more expensive than the transplantation of healthy grafts or grafts with single-vessel disease.

The costs of a straightforward heart transplantation in Germany amount to about 70.000,- € whereas the costs of donor screening angiography are about 800,- €. Since coronary atherosclerosis is common in the present donor pool, screening angiography seems to be a good investment to avoid the loss of about 6 quality-adjusted life years (QALY) by transmitted coronary atherosclerosis (3).

Conclusions

In conclusion, donor screening angiography has to be performed for ethical reasons to reduce the serious risk of the patient of suffering from early graft failure as well as for economic reasons: to avoid substantial cost overruns for the health care system. On the other hand, using screening angiography grafts with limited coronary disease can be gained and therefore the limited donor pool can be expanded by "marginal" donors organs that allow survival rates and health-related quality

of life comparable to those of patients receiving healthy grafts.

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