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Exploring the developmental tasks of emerging adults after pediatric heart transplantation- a cross-sectional case control study

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5 **Exploring the developmental tasks of emerging adults after pediatric**
6 **heart transplantation- a cross-sectional case control study**
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Abstract

Objective

Pediatric heart transplantation (PHTX) comprises 12% of all cardiac transplants and many of the children now survive into adulthood. Only few studies have investigated the long-term psychosocial well-being of young adult patients after PHTX; no studies have investigated developmental tasks of emerging adulthood in different domains (family, social environment, education and profession, partnership, social environment).

Setting

Specialized heart center in Germany.

Participants

Thirty-eight young adults aged 22.11 years (SD=4.7) who underwent PHTX and a control group of 46 participants with no known chronic diseases, aged 22.91 years (SD=1.8), participated in the study.

Outcome measures

All participants completed the following questionnaires: sociodemographic, the F-SozU, to measure perceived social support, the GBB to measure subjective complaints experienced by patients, the KIDSCREEN-27 to measure well-being, and the SF-36 to measure health-related quality of life (QoL).

Results

'Family': the quality of the relationship with the parents was found to be equal in both groups, while PHTX patients stayed in closer spatial proximity to their parents. 'Social environment': PHTX patients reported lower social support by peers than the control group. 'Education and profession': PHTX patients most often worked full-time (23%), had no job and/or received a pension (21%). In comparison, most of the healthy controls did an apprenticeship (40%) and/or worked part time (32%). 'Partnership': fewer of the PHTX patients had a partner than the control group while relationship duration did not differ. In exploratory regression analyses, social support by peers predicted physical QoL, whereas physical complaints and the physical role predicted mental QoL in PHTX patients.

Conclusions

Our exploratory findings highlight important similarities and differences in specific developmental tasks between PHTX patients and healthy controls. Future studies should focus on developmental tasks of PHTX patients in this age group more systematically, investigating their role for physical and mental well-being in a confirmatory manner.

Strength and Limitations

- To our knowledge, this study is one of the first to investigate the developmental tasks in the specific group of emerging adults after PHTX, which has theoretical implications and which is relevant to the psychosocial care of these patients.

- This is a hypothesis-generating study with the unique approach of using well-established questionnaires for the exploration of developmental domains.

- This study is cross-sectional, so no inferences can be made with regard to development across time.

A convenience sample control group was used, which limits generalizability of the results.

- As this was an exploratory study, results should be replicated in confirmatory manner, based on carefully developed hypotheses.

Introduction

Pediatric heart transplantation (PHTX) is an established therapy for end-stage cardiac disease(1) and has increased worldwide to more than 12,000 reported transplants in children since the first procedure in 1967(2). In 2014, a total of 586 heart transplants in children (aged < 18 years) were performed worldwide(3). They comprise 12% of all cardiac transplants reported to the Registry of the International Society for Heart and Lung Transplantation(4). Median survival of children after heart transplantation has increased to about 20 years(5, 6), with the lowest 3-year survival rate in children in Europe under the age of 1 (84.0) and the highest in children between the ages 6 to 10 (89.1)(7, 8). Accordingly, an increasing amount of research focuses on long-term outcomes and quality of life (QoL) after PHTX. Although it is life-saving, it is not curative and children are confronted with chronic health problems(9). Research generally suggests that chronic and/or serious disease in childhood is associated with an increased risk for non-normative physical, psychological and social development(10-12). Serious disease is negatively associated with QoL and identity development of children and adolescents and puts young adults at risk for reduced occupational and social success(13-16). When it comes to PHTX, research shows that it is associated with large improvements in functional status(17). At the same time, a substantial proportion of children and adolescents after PHTX report psychological problems, such as depression, anxiety and behavioral problems(18-22). These psychological problems potentially negatively impact QoL, alongside socio-demographic and medical factors such as renal diseases(23) and infections(24). Later in life, the majority of patients achieve important academic and professional milestones and social well-being(25). A study on adult patients after PHTX reports good QoL and good academic and professional achievement, while patients were most satisfied in the family domain and least satisfied in the psychological and spiritual domain. Most respondents had graduated from high school, reported an average annual income and lived independently(26). Another study focused on the population of young adults (aged 18-25), comparing PHTX patients with two other patient groups (patients with congenital heart disease of moderate severity and patients with congenital heart disease of complex severity). Results showed no differences between the groups in terms of psychosocial maturity, parental fostering of autonomy and transition readiness. Higher psychosocial maturity and parental fostering of autonomy were associated with better perceived mental health and QoL(27). While this study has contributed important insights into psychosocial development of young adults after PHTX, more research into the unique developmental tasks of PHTX patients during emerging adulthood is needed in order to discern a multitude of factors that are potentially relevant to their subjective well-being and QoL.

Emerging adulthood describes a developmental phase of individuals in industrialized countries lasting from the late teens to late twenties, with specific developmental tasks: a) detachment from the

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3 family with spatial (home stay), financial (support from parents) and emotional independence
4 (autonomy experience); b) apprenticeship, training and entering career with the topics of leaving
5 school and finding a job (professional identity); and c), entering romantic relationships (partner
6 selection, building an intimate relationship with a partner)(28-31). In addition, the social
7 environment, especially the peer group, is crucial for well-being and closely linked to the self-
8 reported QoL in this age group(32). In the present study, these developmental tasks in young adults
9 after PHTX were investigated by using well-established questionnaires and by re-grouping subscales
10 and items into developmental domains for exploratory analysis (for an overview, see table 1): a)
11 family (financial and spatial independence, relationship with the parents; b) education and
12 profession (educational level, number of school years, number of missed school years, employment
13 situation, financial situation); c) partnership (marital status, partner status and duration of longest
14 relationship); and d) social environment (social support in general, by peers, feelings about school
15 and social functioning, as well as re-integration at school after PHTX). Furthermore, we looked at
16 subjective physical well-being (specifically, the concept subjective physical complaints comprising the
17 subscales fatigue tendency, gastric complaints, limb pain and heart complaints, as well as the
18 concept physical well-being) and at psychological well-being. Finally, we assessed physical QoL (by
19 means of the SF-36 subscales physical functioning, general health, vitality, physical role, pain and the
20 physical summary scale) and psychological QoL (by means of the SF-36 subscales vitality, social
21 functioning, emotional role, mental health and the mental summary scale), in order to gain an
22 impression of the current subjective health status of the sample.
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36 Table 1. Overview of the instruments we used, clarifying domains and concepts

DOMAIN	CONCEPT	INSTRUMENT	(SUB)SCALE/ ITEM
FAMILY			
	Current living situation	Demographic questionnaire	Living Situation (Item)
	Spatial independence	Demographic questionnaire	Distance from Parents (Item)
	Relationship with the parents	Kidscreen-27	Autonomy & Parent Relation Subscale
EDUCATION AND PROFESSION			
	Educational level	Demographic questionnaire	Highest Completed Education (Item)
	Repeated school years	Demographic	Number of Repeated School

		questionnaire	Years (Item)
	Employment situation	Demographic questionnaire	Current Employment Situation (Item)
	Financial situation	Demographic questionnaire	Maintaining Livelihood (Item)
PARTNERSHIP			
	Marital status	Demographic questionnaire	Marital Status (Item)
	Partner status	Demographic questionnaire	Partner Status (Item)
	Duration of longest relationship	Demographic questionnaire	Duration of Longest Relationship (Item)
SOCIAL ENVIRONMENT			
	Social support in general	F-SozU	F-SozU Total Score
	Social support by peers	Kidscreen-27	Subscale Perceived Social Support & Peers
	Feelings about school	Kidscreen-27	Subscale School
	Social functioning	SF-36	Subscale Self-Rated Social Function
	Re-integration after PHTX	Demographic questionnaire	Re-Integration at School (Item)
SUBJECTIVE PHYSICAL WELL-BEING			
	Subjective physical complaints	GBB	Total Score
	Fatigue Tendency	GBB	Subscale Fatigue Tendency
	Gastric Complaints	GBB	Subscale Gastric Complaints
	Limb Pain	GBB	Subscale Limb Pain
	Heart Complaints	GBB	Subscale Heart Complaints
	Physical well-being	Kidscreen-27	Subscale Physical Well-Being
SUBJECTIVE PSYCHOLOGICAL WELL-BEING			

	Psychological well-being	Kidscreen-27	Subscale Psychological Well-Being
QOL			
	Physical functioning	SF-36	Subscale Physical Functioning
	General health	SF-36	Subscale General Health
	Physical limits in everyday functioning	SF-36	Subscale Physical Role
	Pain	SF-36	Subscale Bodily Pain
	Physical quality of life	SF-36	Physical Summary Scale
	Vitality	SF-36	Subscale Vitality
	Social functioning	SF-36	Subscale Social Functioning
	Emotional limits in everyday functioning	SF-36	Subscale Emotional Role
	Mental health	SF-36	Subscale Mental Health
	Psychological quality of life	SF-36	Mental Summary Scale

Methods

Participant and Public Involvement

A total of 169 children and adolescents underwent a PHTX at the clinic from 1986 to 2010, of which 101 survived. In this cross-sectional study, young adults between the ages of 16 and 35 years who underwent heart transplantation when they were children (< 18 years) at a specialized heart center were eligible for participation. Patients were recruited during the routine medical checks in the hospital. Participation was voluntary. The study was approved by the Medical Ethics Committee Charité Mitte (Nr.EA2/002/10). Fifty-two eligible patients met the inclusion criteria, of whom 38 agreed to participate in the study.

Participants were approached via telephone/mail and informed about the study. If interested in participation, they received an information letter from the research team about the objectives, design and procedure of the study. Informed consent was obtained from all participants via mail. After that, participants received questionnaires on paper, a stamped envelope and a letter with instructions on how to fill out and return the questionnaires via mail. Patients were instructed to fill out the questionnaires at home and to return the completed questionnaires using the stamped envelope.

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3 A comparison group of 46 young healthy controls between the ages of 19 and 26 years with no
4 known chronic diseases was recruited via social networks and personal contacts. Eligible participants
5 were contacted by phone, e-mail or personally. Informed consent of each participant was obtained;
6 participants then received the questionnaires via e-mail, mail (together with a stamped envelope), or
7 in person. Questionnaires were returned via mail or in person.
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10 Outcome had been determined for all patients who previously asked for results by the end of the
11 data collection (December 2016). Due to the exploratory design, the development of the research
12 question was not informed by patients' priorities, experience, and preferences.
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17 Inclusion Criteria PHTX patients:

- 18 - PHTX at the clinic from 1986 to 2010
- 19 - Current age between 16 and 35 years

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21 Inclusion Criteria healthy controls:

- 22 - Young adults between the ages of 16 and 35 years
- 23 - No known chronic disease

24 25 26 27 **Instruments**

28 29 *Demographics*

30 Demographic information was obtained via a questionnaire developed by the research team with the
31 following items: marital status, partner status, duration of longest relationship, living situation,
32 distance from parents' home, educational level, number of repeated school years, current
33 employment situation, maintaining livelihood, successful re-integration at school after PHTX. For an
34 overview of items used for the analysis of each developmental domain, see table 1. Additionally, the
35 variables age, sex and date of transplantation were obtained from medical records.
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41 42 *Social Support Questionnaire- Short Form*

43 The German version of the Social Support Questionnaire-Short Form (Fragebogen zur Sozialen
44 Unterstützung; F-SozU, K-14) was used, which is a 14-item self-report of subjectively perceived or
45 anticipated social support. A total score can be computed, which ranges from 1 to 5 and which was
46 used for the analysis of the domain 'social environment'; see table 1. Psychometric properties are
47 good (33).
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51 52 *Giessen Complaints Inventory*

53 The German version of the Giessen Complaints Inventory (Gießener Beschwerde-Bogen, GBB) by
54 Brähler and Scheer (1995) was used. The GBB is an instrument for physical complaints frequently
55 used in Germany which measures subjective limitations experienced by patients due to their physical
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3 symptoms. The questionnaire comprises 24 items and contains the following subscales: fatigue
4 tendency, gastric complaints, limb pain and heart complaints. Scores per subscale range from 0 to 24.
5 A total score (general discomfort) can be computed, which ranges from 0 to 96 points. The total
6 score was used for the analysis of the domain 'subjective physical well-being'. Psychometric
7 properties are good.
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10 11 12 *Kidscreen-27*

13 The KIDSCREEN-27 by Ravens-Sieberer et al. (2005) is a German questionnaire for health-related QoL
14 specifically developed for children. It measures the following five subscales: 'autonomy and parent
15 relations', which we used in the domain 'family', 'perceived social support & peers' and 'school', both
16 of which we used in the domain 'social environment'; 'physical well-being' and 'psychological well-
17 being', which we used in the domains 'subjective physical well-being' and 'subjective psychological
18 well-being' (see table 1). Scores per subscale range from 0 to 100, with a higher score indicating a
19 better QoL. A total score can be computed ranging from 0 to 100 points. Psychometric properties are
20 good (34).
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26 27 28 *Short-Form -36-Item Health Survey*

29 The German Version of the Short-Form-36 (SF-36) by Bullinger and Kirchberger (1998) was used,
30 which is a generic health survey comprising 36 items in eight subscales (physical functioning, role
31 functioning physical, bodily pain, general health perceptions, vitality, social functioning, role
32 functioning emotional and mental health). We subsumed each of the subscales into the domains
33 'subjective physical well-being' and 'subjective psychological well-being', as appropriate (see table 1).
34 The subscales can be aggregated into two component summary scores representing the physical
35 summary scale and the mental summary scale, both of which we used in the domain 'quality of life'
36 (see table 1). Subscale and summary scores range from 0 to 100, based on transformed z-scores with
37 multiplication of the regression coefficients of the normative sample. A higher score indicates a
38 better QoL. Psychometric properties are good (35).
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46 **Analysis**

47 IBM SPSS Statistics 23 was used for descriptive and inferential statistics. A p-value of ≤ 0.05 was
48 considered statistically significant. Chi-square tests for dichotomous variables, t-tests and univariate
49 analyses of variance were performed for exploratory group comparisons in all developmental
50 domains (for an overview of developmental domains, see table 1). Univariate regressions were
51 conducted for exploratory analyses of predictors of physical and psychological QoL.
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Results

Sample characteristics

All 38 participants of the PHTX group underwent heart transplantation when they were children, with a mean age at time of transplantation of 10.95 years (SD=3.7). The mean age at time of recruitment was 22.11 years (SD=4.7), ranging from 16 to 35 years. Fifty percent of the patients were male. The mean waiting time for an organ was 0.47 years (SD=0.5). Number of years between PHTX and assessment was on average 11.16 years (SD=5.3), ranging from 4 to 23 years.

In the control group, mean age at assessment was 22.91 years (SD=1.8), ranging from 19 to 26 years; 45 percent were male.

Between groups, there are no significant differences in age ($F(1,45,67) = 1.00, p = 0.285$) or gender ($\chi^2(1, N=84) = 1.98, p=0.159$). Regarding the educational level, the control group was significantly more highly educated than the PHTX patients ($t(80) = -16.313, p < 0.001$, high school or university in 96% and 8%, respectively). Furthermore, the control group individuals reported being in a partnership more often than the PHTX patients ($\chi^2(1, N=84) = 9.42, p = 0.002$, 65% and 32%, respectively).

Family

In this domain, we focused on the current living situation, spatial independence and relationship with the parents, with the following results: The living situation differs significantly between the PHTX and control group, $t(46,19) = -2.22, p = 0.031$. Twenty-one of the PHTX patients (55%) lived with their parents, while the remaining 45% had moved out. Of those 45%, 18% lived with their partner, 11% lived alone, 11% lived next to their parents in a separate apartment and 5% shared a flat. By contrast, only 22% of the control group lived with their parents, while 78% had moved out, see table 2.

In the subgroup of participants who no longer live with their parents, the distance to the parents' home in km differs significantly between the groups ($F(1,26,0) = 45.57, p < 0.001$). The PHTX stay closer to their parents' house ($M=1.66\text{km}, SD=1.26\text{km}$), while the healthy controls move further away ($M=213.37\text{km}, SD=280.99\text{km}$).

The perceived quality of the relationship with their parents and self-estimated autonomy are reported differently in the two groups ($F(1,57) = 5.72, p = 0.02$), with higher scores reported by the PHTX group than by the control group, indicating higher perceived quality of the relationship and perceived autonomy in the PHTX group, see table 2.

Table 2. Characteristics and metrics of family variables in the PHTX group and control group

Characteristic	assessed by	Value	PHTX (N=38)	Control group (N=46)	p
Living	Social	With parents	21 (55%)	10 (22%)	0.031

situation	demographic questionnaire	With partner	7 (18%)	9 (20%)	
		Alone	4 (11%)	10 (21%)	
		Next to parents	4 (11%)	0	
		Flat share	2 (5%)	17 (37%)	
Distance to parents' home in km	Social demographic questionnaire	Mean	1.66	213.37	< 0.001
		SD	1.26	280.99	
Relation to parents and autonomy	KIDSCREEN-27	Mean	59.15	53.49	0.020
		SD	9.27	7.78	

Education and profession

In this domain, we focused on the number of repeated school years, the educational level, employment situation and financial situation. The educational level differs significantly between the two groups ($t(79) = -11.42, p < 0.001$): the PHTX patients less often completed high school education than healthy controls (52% and 96%, respectively), fewer of them were currently studying (3% and 62%, respectively) and a smaller percentage achieved an academic degree (5% and 33%, respectively). Three PHTX patients (8%) had dropped out of school, as opposed to no participants from the healthy control group. At school, the PHTX group had to repeat a grade significantly more often than the control group ($\chi^2(1, N=80) = 20.53, p < 0.001$). Ten PHTX patients (26%) repeated one school year and three PHTX patients (8%) repeated two school years, while none of the control group repeated a school year.

The type of the current job also differs between the two groups ($\chi^2(1, N=79) = 26.36, p < 0.001$), with PHTX patients having part-time jobs less often than the control group (9% and 34%, respectively). The PHTX group's occupations are distributed between jobs in full time (23%), training (11%), apprenticeship (17%), unemployed (23%), retired (11%), half time jobs (3%) or part time jobs (6%) and other (6%). The control group reported the following occupations: full time (5%), training (2%), apprenticeship (40%), unemployed (5%), half time jobs (2%), part time jobs (32%) and other (14%). Finally, sources of financial support differ between the groups ($t(52.68) = 3.46, p=0.001$): sources of income are more widely distributed in PHTX patients, in comparison with the control group (see table 3). Thirty-four percent of the PHTX group reported being financially independent because of a paid job, as opposed to 64% of the control group. Furthermore, PHTX patients less often receive financial support from their parents than the control group ($\chi^2(1, N=80) = 11.75, p = 0.001$).

Table 3.

Characteristics and metrics of school, apprenticeship and financial variables in PHTX and control group

characteristics	Value	PHTX (N=38)	control group (N=46)	p
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Repeated years at school	Yes	14 (37%)	0	< 0.001
	No	21 (55%)	46	
Number of repeated years at school	0	20 (53%)	46	< 0.001
	1	10 (26%)	0	
	2	3 (8%)	0	
Education level	Still attending school	4 (10%)	0	< 0.001
	No exam	3 (8%)	0	
	School for children with learning difficulties	5 (13%)	0	
	Secondary school level	22 (58%)	1 (2%)	
	A-level	1 (3%)	27 (59%)	
	College	1 (3%)	0	
Current job	University	1 (3%)	15 (33%)	< 0.001
	Full time	8 (21%)	2 (4%)	
	Half time	1 (3%)	1 (2%)	
	Part time	2 (5%)	14 (30%)	
	Training	4 (11%)	1 (2%)	
	Apprenticeship	6 (16%)	18 (39%)	
	Unemployed	8 (21%)	2 (4%)	
	Retired	4 (11%)	0	
Financial life (multiple choice)	Other	2 (5%)	6 (13%)	0.001
	Own money via job	13 (34%)	30 (65%)	
	Parents/family members	15 (39%)	37 (80%)	
	Dole	5 (13%)	0	
	Pension	8 (21%)	0	
	Welfare	4 (11%)	0	
	Others	4 (11%)	8 (17%)	

Partnership

In this domain, we focused on marital status, partner status and the duration of the longest relationship. The marital status differs significantly between the two groups ($\chi^2 (1, N=84) = 14.34, p = 0.002$): 92% of the PHTX patients reported being single, 5% were married and 3% divorced. In comparison, 100% of the control group were single and none were married or divorced. In the subgroup of single participants, 65% of the PHTX patients and 32% of the control group reported having a partner ($\chi^2 (1, N=84) = 9.42, p = 0.002$). The duration of the longest relationship does not differ between groups ($F(1,75) = 1.52, p = 0.222$); see table 4 for an overview.

Table 4.

Characteristics and metrics of partnership in PHTX and control group

Characteristics	Value	PHTX (N=38)	Healthy controls (N=46)	p
Marital status	Single	35 (92%)	46 (100%)	0.002
	Divorced	1 (3%)	0	
	Married	2 (5%)	30 (65%)	
			0	
Partnership	Yes	12 (32%)	30 (65%)	0.002

	No	26 (68%)	16 (35%)	
Duration of longest relationship (in months)	Mean	23.45	31.67	0.222
	SD	25.81	29.36	

Social environment

In this domain, we focused on social support in general, social support by peers, feelings about school, re-integration after PHTX, as well as the self-rated social function, with the following results. The PHTX group was asked if re-integration at school after HTX was 'successful or not' (dichotomous variable) as part of the demographic questionnaire. Fifty-eight percent reported the reentry into school as not successful. The total score of the F-SozU differs between the groups ($F(1,44.92) = 23.39$, $p < 0.001$), with the control group reporting higher perceived social support than the PHTX group. On the KIDSCREEN-27 subscale 'social support by peers', the PHTX group scored lower than the control group ($F(1,75) = 1.52$, $p = 0.22$), indicating less perceived support by their peer group. On the SF-36 subscale 'social functioning', the PHTX group also scored lower than healthy controls ($F(1,82) = 6.11$, $p = 0.015$), indicating poorer social functioning, see table 5.

Table 5.
Social support of PHTX patients and control group

Characteristics	Assessed by	Value	PHTX (N=46)	control group (N=38)	P
Integration in school	Social demographic questionnaire	Successful	16 (42%)		
		Not successful	22 (58%)		
Social support	F-SozU	Mean	4.31	4.77	< 0.001
		SD	0.65	0.28	
Social support by peers	KIDSCREEN-27	Mean	45.5	50.38	0.046
		SD	10.98	7.39	
Feelings about school	KIDSCREEN-27	Mean	50.90	51.19	0.901
		SD	9.47	6.37	
Social functioning	SF-36	Mean	80.59	91.03	0.022
		SD	24.26	13.86	

Subjective well-being and quality of life

In this domain we focused on different aspects of subjective physical well-being (subjective physical complaints, physical functioning, general health, physical limits in everyday functioning, pain and physical well-being), psychological well-being (psychological well-being, vitality, social functioning and emotional limits in everyday functioning) as well as the physical and psychological QoL.

Subjective physical well-being. Subjective physical complaints, as assessed with the GBB total score, do not differ between the two groups ($F(1,83) = 0.78$, $p = 0.379$). On a subscale level, a significant difference was found on the subscale fatigue tendency ($F(1,83) = 4.39$, $p = 0.039$), with PHTX patients

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3 reporting more fatigue symptoms than the control group (M=3.0, SD=2.79 and M=1.91, SD=1.95,
4 respectively). No differences were found on the subscales of gastric complaints, limb pain or heart
5 complaints. On the subscale physical well-being of the Kidscreen-27, no significant difference was
6 observed between groups ($t(60) = -1.91, p = 0.06$).

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10 **Subjective psychological well-being.** No significant difference on the Kidscreen-27 subscale
11 'psychological well-being' was observed between groups ($t(60) = -1.98, p = 0.052$).

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15 **QoL.** The PHTX patients reported a lower level of physical QoL based on the physical summary scale
16 of the SF-36 than the control group ($F(1,43.54) = 14.51, p < 0.001$). Also, the PHTX patients scored
17 lower in all physical subscales than the control group (physical functioning: $F(1,82)=21.69, p<0.001$;
18 role physical: $F(1,78)=7.92, p=0.006$; bodily pain: $F(1,82)=6.04, p=0.016$; general health: $F(1,78)=4.9,$
19 $p=0.03$) (see figure 1).

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25 However, the PHTX patients showed no differences in psychological QoL, based on the mental
26 summary scale of the SF-36 ($F(1,76) = 0.15, p = 0.70$). On the subscale-level, only 'social functioning'
27 differed between the groups ($F(1,82) = 6.11, p = 0.015$), with a lower score reported by the PHTX
28 patients (see figure 2).

29 30 31 32 **Predictors of physical and mental quality of life in PHTX patients**

33 To explore which factors predict QoL (psychological and physical) in PHTX patients, we correlated all
34 variables (from the domains family, education and profession, partnership, social environment and
35 subjective well-being) with the physical and psychological component summary scores of the SF-36
36 as a first step. Based on significant exploratory correlations, variables were then selected as
37 predictors for each of the two scales. Regression assumptions were checked and met for both
38 regressions. Next, we calculated two stepwise univariate regression models (one for each summary
39 scale of the SF-36). Variables were included stepwise as independent variables in the regression
40 model. In order to avoid overfitting the model, all SF-36 subscales comprising the physical QoL
41 component were excluded from the regression analysis, with the physical summary scale as criterion.
42 All SF-36 subscales comprising psychological QoL were excluded from the analysis, with the mental
43 summary scale as criterion.

44 45 46 47 48 49 50 **Predictors of physical quality of life**

51 The following predictors were entered in the first regression model, with physical QoL entered as
52 criterion: 1) school re-integration ($r=0.497, p=0.01$); 2) physical complaints ($r=-0.381, p=0.035$); 3)
53 vitality ($r= 0.369, p=0.041$); 4) social support by peers ($r=0.771, p<0.001$); and 5) subjective physical
54 and psychological well-being ($r=0.595, p=0.012$; respectively $r =0.520, p=0.033$). The analyses

revealed that better social support by peers (comprising, for instance, the items 'have you spent time with your friends?' or 'have you and your friends helped each other') predicts a higher physical QoL in PHTX patients, explaining 58.9% of variance ($p=0.001$). See table 6 for the full regression model.

Predictors of psychological QoL

The following predictors were entered in the second regression model, with psychological QoL as criterion: 1) duration of longest relationship ($r=-0.455$, $p=0.022$); 2) distance from parents' home ($r=-0.443$, $p=0.013$); physical complaints ($r=-0.491$, $p=0.005$); 3) role physical ($r=0.498$, $p=0.005$) and 4) subjective psychological well-being ($r=0.683$, $p=0.003$). The analysis revealed two significant predictors: fewer physical complaints and a better role functioning predicted better psychological QoL in PHTX patients, explaining 89.0% of variance ($p<0.001$). See table 6 for the best fitting model.

Table 6.
Stepwise linear univariate regression model: predictors of QoL (n=38)

Criterion	Predictor	B	SE	p	95% C.I. for B	
					Lower	Upper
Physical QoL	Peers (KIDSCREEN-27)	0.65	0.15	0.001	0.34	0.96
	Constant	20.73	6.95	0.001	5.81	35.64
Mental QoL	Physical Complaints (GBB)	-0.33	0.09	0.007	-0.54	-0.12
	Role Physical (physical subscale SF-36)	0.26	0.10	0.036	0.02	0.51
	Constant	28.79	10.37	0.027	4.27	53.31

Discussion

In this study, we explored developmental tasks of emerging adulthood in a sample of young adults after PHTX in an exploratory manner. The following categories were examined: a) family (current living situation, spatial independence, relationship with the parents) b) education and profession (educational level, repeated school years, employment situation, financial situation) c) partnership (marital status, partner status and duration of longest relationship) and d) social environment (perceived social support in general, by peers, feelings about school, social functioning, and re-integration at school after PHTX). Additionally, subjective physical well-being, subjective psychological well-being and QoL (physical and psychological) were assessed. Finally, we investigated which of the variables from domains a-d, as well as variables from the domains subjective physical and psychological well-being predict self-reported QoL.

In comparison to our control group, PHTX patients more often live with their parents and when they move out, they stay in closer proximity to their parents. We found no differences in the perceived quality of the relationship with the parents.

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3 When it comes to financial independence, the PHTX patients rely less on their family for financial
4 support than the control group. PHTX patients held full-time positions more frequently than the
5 control group, while healthy controls more often chose part time work. Importantly, a significant
6 percentage of PHTX patients had no job and/or received a pension. As PHTX patients more frequently
7 had to repeat at least one school year, probably due to health problems and hospital stays, the
8 choice of full-time work, which might reflect the choice for non-academic career paths, might be
9 related to more academic difficulties related to their disease. Future studies should focus on this
10 issue, systematically investigating academic disadvantages and choices due to underlying disease and
11 the challenges that come with PHTX.
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17 When it comes to partnership, more PHTX patients reported being single than healthy individuals
18 from the control group, even though the groups did not differ in age. However, the duration of the
19 longest relationship did not differ between groups. This finding might be due to difficulties in
20 initiating partnership, while partnership stability is not compromised in PHTX patients once they have
21 found a partner. PHTX patients in our sample reported less perceived social support in general and
22 by their peers. Social contacts are of great importance for teenagers and young adults. Facilitating
23 social relationships in order to increase well-being and QoL of this vulnerable group might be an
24 important goal for psychosocial reintegration in patients after PHTX. Future studies should take a
25 closer look at social relationships in this group, focusing on number of social relationships, as well as
26 quality and stability of their social networks.
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32 PHTX patients reported a higher fatigue tendency than the control group, while no differences were
33 found in other areas of physical complaints. Symptoms of fatigue might limit PHTX patients' activities
34 in daily life and hinder participation in social life, leisure activities etc. This finding also warrants
35 further investigation.
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39 PHTX patients reported equal psychological well-being to the control group, which is a favorable
40 result. However, they did report lower a physical QoL. In our exploratory regression models, we
41 found that better perceived social support by peers predicts a better physical QoL, with a high
42 proportion of explained variance. While these results further emphasize the importance of peer
43 relations in this age group, the relationship between physical well-being and peer relations should be
44 investigated further. Finally, we found that fewer physical complaints predict a better mental QoL,
45 also with a large proportion of explained variance. In sum, PHTX patients fare well when it comes to
46 their financial autonomy, relationship with their parents and profession, while they only rarely
47 choose an academic career. They report lower social support in general and from peers and have
48 more physical complaints (fatigue tendency), as well as reduced physical QoL, which both seem to be
49 intertwined with social support from peers. While, on average, their mental well-being is comparable
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3 to that of the control group, fewer physical complaints predict higher scores on the mental well-
4 being scale, also pointing to the key role of their physical health for other domains of functioning.
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6 Importantly, this study is cross-sectional and exploratory and the results should be cautiously
7 interpreted. Future studies investigating developmental challenges of PHTX patients during emerging
8 adulthood should be longitudinal, in order to shed light on psychosocial adjustment after PHTX
9 across time. Control groups should be carefully matched according to key variables, while hypotheses
10 should be carefully developed and tested in a confirmatory manner.
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21 Conflict of interests

22 None
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24
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26 Author's contribution

27 Maria Sepke and Wolfgang Albert made substantial contributions to the conception and design of
28 the work. Maria Sepke and Hannah Ferentzi contributed to manuscript drafting and editing. Maria
29 Sepke, Hannah Ferentzi, Vera Disselhoff and Wolfgang Albert reviewed the protocol and made
30 amendments. All authors critically reviewed and approved the final version. All authors agree to be
31 accountable for all aspects of the work.
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37 Data statement section

38 We plan to publish the raw data with 'Dryad' when data sharing is desired.
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42 Funding

43 This research received no specific grant from any funding agency in the public, commercial or not-
44 for-profit sectors.'
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48 Figure legend

49
50 Figure 1. Means of z-transformed scores of the SF-36 physical summary scale and all physical
51 subscales raw values 0–100 of PHTX and control group.
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53 Figure 2. Means of z-transformed scores of the SF-36 mental summary scale and all psychological
54 subscales raw values 0–100 of PHTX and control group.
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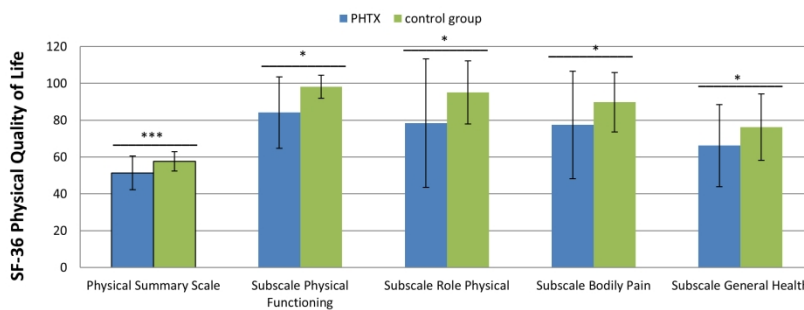


Figure 1. Means of z-transformed scores of the SF-36 physical summary scale and all physical subscales raw values 0–100 of PHTX and control group.

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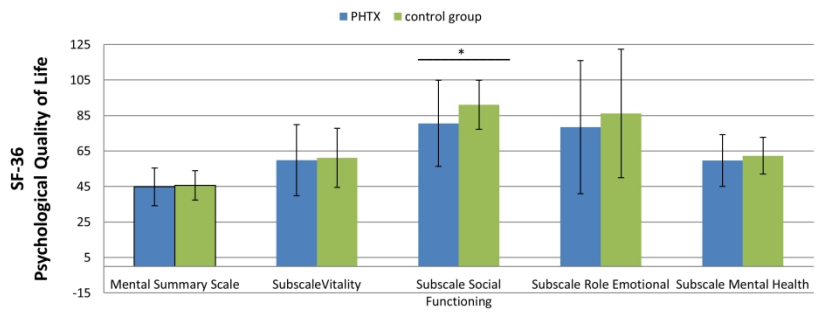


Figure 2. Means of z-transformed scores of the SF-36 mental summary scale and all psychological subscales raw values 0–100 of PHTX and control group.

254x190mm (300 x 300 DPI)

Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE case-control reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale	5

1		for the choice of cases and controls. For matched studies, give	
2		matching criteria and the number of controls per case	
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4		#6b For matched studies, give matching criteria and the number of	n/a
5		controls per case	
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8		#7 Clearly define all outcomes, exposures, predictors, potential	7
9		confounders, and effect modifiers. Give diagnostic criteria, if	
10		applicable	
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13	Data sources /	#8 For each variable of interest give sources of data and details of	6
14	measurement	methods of assessment (measurement). Describe	
15		comparability of assessment methods if there is more than one	
16		group. Give information separately for cases and controls.	
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20	Bias	#9 Describe any efforts to address potential sources of bias	n/a
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22	Study size	#10 Explain how the study size was arrived at	5
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24	Quantitative	#11 Explain how quantitative variables were handled in the	6
25	variables	analyses. If applicable, describe which groupings were	
26		chosen, and why	
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30	Statistical	#12a Describe all statistical methods, including those used to control	7
31	methods	for confounding	
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34		#12b Describe any methods used to examine subgroups and	7
35		interactions	
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38		#12c Explain how missing data were addressed	7
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40		#12d If applicable, explain how matching of cases and controls was	7
41		addressed	
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44		#12e Describe any sensitivity analyses	7
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46	Participants	#13a Report numbers of individuals at each stage of study—eg	7
47		numbers potentially eligible, examined for eligibility, confirmed	
48		eligible, included in the study, completing follow-up, and	
49		analysed. Give information separately for cases and controls.	
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53		#13b Give reasons for non-participation at each stage	7
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55		#13c Consider use of a flow diagram	n/a
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57	Descriptive data	#14a Give characteristics of study participants (eg demographic,	7
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1		clinical, social) and information on exposures and potential	
2		confounders. Give information separately for cases and	
3		controls	
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6		#14b Indicate number of participants with missing data for each	n/a
7		variable of interest	
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9	Outcome data	#15 Report numbers in each exposure category, or summary	7-11
10		measures of exposure. Give information separately for cases	
11		and controls	
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14	Main results	#16a Give unadjusted estimates and, if applicable, confounder-	7-11
15		adjusted estimates and their precision (eg, 95% confidence	
16		interval). Make clear which confounders were adjusted for and	
17		why they were included	
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21		#16b Report category boundaries when continuous variables were	7-11
22		categorized	
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25		#16c If relevant, consider translating estimates of relative risk into	7-11
26		absolute risk for a meaningful time period	
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29	Other analyses	#17 Report other analyses done—e.g., analyses of subgroups and	n/a
30		interactions, and sensitivity analyses	
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33	Key results	#18 Summarise key results with reference to study objectives	11
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35	Limitations	#19 Discuss limitations of the study, taking into account sources of	12
36		potential bias or imprecision. Discuss both direction and	
37		magnitude of any potential bias.	
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40	Interpretation	#20 Give a cautious overall interpretation considering objectives,	11-12
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42		and other relevant evidence.	
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45	Generalisability	#21 Discuss the generalisability (external validity) of the study	12
46		results	
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49	Funding	#22 Give the source of funding and the role of the funders for the	13
50		present study and, if applicable, for the original study on which	
51		the present article is based	
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BMJ Open

Exploring the developmental tasks of emerging adults after pediatric heart transplantation- a cross-sectional case control study

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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Paediatrics, Mental health, Global health
Keywords:	heart transplantation, developmental tasks, Paediatric cardiology < CARDIOLOGY, Quality of Life, psychosocial

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5 **Exploring the developmental tasks of emerging adults after pediatric**
6 **heart transplantation- a cross-sectional case control study**
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11 Maria Sepke^{1,2,3}, Hannah Ferentzi⁴, Vera Stéphanie Umutoni Disselhoff³, Wolfgang Albert^{1,3,5}

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49 Keywords: heart transplantation, developmental tasks, emerging adults, pediatric, psychosocial
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53 Word count: 4.054 (excluding the title page, abstract, references, tables, boxes, or figures)
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Abstract

Objective

Pediatric heart transplantation (PHTX) comprises 12% of all cardiac transplants and many of the children now survive into adulthood. Only a few studies have investigated the long-term psychosocial well-being of young adult patients after PHTX; no studies have investigated developmental tasks of emerging adulthood in different domains (family, social environment, education and profession, partnership, social environment).

Setting

Specialized heart center in Germany.

Participants

Thirty-eight young adults aged 22.11 years (SD=4.7) who underwent PHTX and a control group of 46 participants with no known chronic diseases, aged 22.91 years (SD=1.8), participated in the study.

Outcome measures

All participants completed the following questionnaires: sociodemographic, the F-SozU, to measure perceived social support, the GBB to measure subjective complaints experienced by patients, the KIDSCREEN-27 to measure well-being, and the SF-36 to measure health-related quality of life (QoL).

Results

'Family': the quality of the relationship with the parents was found to be equal in both groups, while PHTX patients stayed in closer spatial proximity to their parents. 'Social environment': PHTX patients reported lower social support by peers than the control group. 'Education and profession': PHTX patients most often worked full-time (23%), had no job and/or received a pension (21%). In comparison, most of the healthy controls did an apprenticeship (40%) and/or worked part time (32%). 'Partnership': fewer of the PHTX patients had a partner than the control group while relationship duration did not differ. In exploratory regression analyses, social support by peers predicted physical QoL, whereas physical complaints and the physical role predicted mental QoL in PHTX patients.

Conclusions

Our exploratory findings highlight important similarities and differences in specific developmental tasks between PHTX patients and healthy controls. Future studies should focus on developmental tasks of PHTX patients in this age group more systematically, investigating their role in physical and mental well-being in a confirmatory manner.

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Strengths and limitations

- To our knowledge, this study is one of the first to investigate the developmental tasks in the specific group of emerging adults after PHTX to have theoretical implications and which is relevant to the psychosocial care of these patients.

- This is a hypothesis-generating study with the unique approach of using well-established questionnaires for the exploration of developmental domains.

- This study is cross-sectional, so no inferences can be made with regard to development over time.

A convenience sample control group was used, which limits generalizability of the results.

- As this was an exploratory study, results should be replicated in confirmatory manner, based on carefully developed hypotheses.

Introduction

Pediatric heart transplantation (PHTX) is an established therapy for end-stage cardiac disease (1) and has increased worldwide to more than 12,000 reported transplants in children since the first procedure in 1967 (2). In 2014, a total of 586 heart transplants in children (aged < 18 years) were performed worldwide (3). They comprise 12% of all cardiac transplants reported to the Registry of the International Society for Heart and Lung Transplantation (4). Median survival of children after heart transplantation has increased to about 20 years (5,6), with the lowest 3-year survival rate in children in Europe under the age of 1 (84.0) and the highest in children between the ages 6 to 10 (89.1)(7,8). Accordingly, an increasing amount of research focuses on long-term outcomes and quality of life (QoL) after PHTX. Although it is life-saving, it is not curative and children are confronted with chronic health problems (9). Research generally suggests that chronic and/or serious disease in childhood is associated with an increased risk for non-normative physical, psychological and social development (10-12). Serious disease is negatively associated with QoL and identity development of children and adolescents and puts young adults at risk for reduced occupational and social success (13-16). When it comes to PHTX, research shows that it is associated with large improvements in functional status (17). At the same time, a substantial proportion of children and adolescents after PHTX report psychological problems, such as depression, anxiety and behavioral problems (18-22). These psychological problems potentially negatively impact QoL, alongside socio-demographic and medical factors such as renal diseases (23) and infections (24). Later in life, the majority of patients achieve important academic and professional milestones and social well-being (25). A study on adult patients after PHTX reports good QoL and good academic and professional achievement, while patients were most satisfied in the family domain and least satisfied in the psychological and spiritual domain. Most respondents had graduated from high school, reported an average annual income and lived independently (26). Another study focused on the population of young adults (aged 18-25) comparing PHTX patients with two other patient groups (patients with congenital heart disease of moderate severity and patients with congenital heart disease of complex severity). Results showed no differences between the groups in terms of psychosocial maturity, parental fostering of autonomy and transition readiness. Higher psychosocial maturity and parental fostering of autonomy were associated with better perceived mental health and QoL (27). While this study has contributed important insights into psychosocial development of young adults after PHTX, more research into the unique developmental tasks of PHTX patients during emerging adulthood is needed in order to discern a multitude of factors that are potentially relevant to their subjective well-being and QoL.

Emerging adulthood describes a developmental phase of individuals in industrialized countries lasting from the late teens to late twenties, with specific developmental tasks: a) detachment from the family with spatial (home stay), financial (support from parents) and emotional independence (autonomy experience); b) apprenticeship, training and entering career with the topics of leaving school and finding a job (professional identity); and c), entering romantic relationships (partner selection, building an intimate relationship with a partner) (28-31). In addition, the social environment, especially the peer group, is crucial for well-being and closely linked to the self-reported QoL in this age group (32). In the present study, these developmental tasks in young adults after PHTX were investigated by using well-established questionnaires and by re-grouping subscales and items into developmental domains for exploratory analysis listed in table 1. Furthermore, we looked at subjective physical well-being (specifically, the concept subjective physical complaints comprising the subscales fatigue tendency, gastric complaints, limb pain and heart complaints, as well as the concept physical well-being) and at psychological well-being. Finally, we assessed physical QoL (by means of the SF-36 subscales physical functioning, general health, vitality, physical role, pain and the physical summary scale) and psychological QoL (by means of the SF-36 subscales vitality, social functioning, emotional role, mental health and the mental summary scale), in order to gain an impression of the current subjective health status of the sample.

Table 1. Overview of the instruments we used, clarifying domains and concepts

DOMAIN	CONCEPT	INSTRUMENT	(SUB)SCALE/ ITEM
FAMILY			
	Current living situation	Demographic questionnaire	Living Situation (Item)
	Spatial independence	Demographic questionnaire	Distance from Parents (Item)
	Relationship with the parents	Kidscreen-27	Autonomy & Parent Relation Subscale
EDUCATION AND PROFESSION			
	Educational level	Demographic questionnaire	Highest Completed Education (Item)
	Repeated school years	Demographic	Number of Repeated School

		questionnaire	Years (Item)
	Employment situation	Demographic questionnaire	Current Employment Situation (Item)
	Financial situation	Demographic questionnaire	Maintaining Livelihood (Item)
	PARTNERSHIP		
	Marital status	Demographic questionnaire	Marital Status (Item)
	Partner status	Demographic questionnaire	Partner Status (Item)
	Duration of longest relationship	Demographic questionnaire	Duration of Longest Relationship (Item)
	SOCIAL ENVIRONMENT		
	Social support in general	F-SozU	F-SozU Total Score
	Social support by peers	Kidscreen-27	Subscale Perceived Social Support & Peers
	Feelings about school	Kidscreen-27	Subscale School
	Social functioning	SF-36	Subscale Self-Rated Social Function
	Re-integration after PHTX	Demographic questionnaire	Re-Integration at School (Item)
	SUBJECTIVE PHYSICAL WELL-BEING		
	Subjective physical complaints	GBB	Total Score
	Fatigue Tendency	GBB	Subscale Fatigue Tendency
	Gastric Complaints	GBB	Subscale Gastric Complaints
	Limb Pain	GBB	Subscale Limb Pain
	Heart Complaints	GBB	Subscale Heart Complaints
	Physical well-being	Kidscreen-27	Subscale Physical Well-Being
	SUBJECTIVE		

PSYCHOLOGICAL WELL-BEING			
	Psychological well-being	Kidscreen-27	Subscale Psychological Well-Being
QOL			
	Physical functioning	SF-36	Subscale Physical Functioning
	General health	SF-36	Subscale General Health
	Physical limits in everyday functioning	SF-36	Subscale Physical Role
	Pain	SF-36	Subscale Bodily Pain
	Physical quality of life	SF-36	Physical Summary Scale
	Vitality	SF-36	Subscale Vitality
	Social functioning	SF-36	Subscale Social Functioning
	Emotional limits in everyday functioning	SF-36	Subscale Emotional Role
	Mental health	SF-36	Subscale Mental Health
	Psychological quality of life	SF-36	Mental Summary Scale

Methods

Participants

Group of PHTX patients

A total of 169 children and adolescents underwent a PHTX at our hospital from 1986 to 2010, of which 101 survived. In this cross-sectional study, young adults between the ages of 16 and 35 years who underwent heart transplantation when they were children (< 18 years) at a specialized heart center were eligible for participation. Patients were recruited during the routine medical checks in the hospital. Participation was voluntary. The study was approved by the Medical Ethics Committee Charité Mitte (Nr.EA2/002/10). Fifty-two eligible patients met the inclusion criteria, of whom 38 agreed to participate in the study.

If interested in participation, they received an information letter from the research team about the objectives, design and procedure of the study. Informed consent was obtained from all participants via

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3 mail. After that, participants received questionnaires on paper, a stamped envelope and a letter with
4 instructions on how to fill out and return the questionnaires via mail. Patients were instructed to fill out
5 the questionnaires at home and to return the completed questionnaires using the stamped envelope.
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10 Inclusion criteria for PHTX patients:

- 11 - PHTX at our hospital from 1986 to 2010
 - 12 - Current age between 16 and 35 years
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16 *Group of healthy controls*

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18 A comparison group of 46 young healthy controls between the ages of 19 and 26 years with no known
19 chronic diseases was recruited via social networks and personal contacts. We ensured that the control
20 group had the same mean age and gender distribution as the PHTX group. Eligible participants were
21 recruited via social network and personal contacts and, if interested in participation, were contacted by
22 phone, e-mail or personally. Informed consent of each participant was obtained; participants then
23 received the questionnaires via e-mail, mail (together with a stamped envelope), or in person.
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25 Questionnaires were returned via mail or in person.
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29 Outcomes had been determined for all patients who previously asked for results by the end of the data
30 collection (December 2016). Due to the exploratory design, the development of the research question
31 was not informed by patients' priorities, experience, and preferences.
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36 Inclusion criteria for healthy controls:

- 37 - Young adults between the ages of 16 and 35 years
 - 38 - No known chronic disease
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42 *Patients and public involvement*

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44 The study was designed to understand patients' experience and to observe developmental tasks of
45 young adults after pediatric heart transplantation. However, patients were not included in the design of
46 the survey, recruitment or conduct of the study. Patients were informed about the option to be
47 debriefed about the study results after completion of the study.
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50 *Instruments*

51 *Demographics*

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53 Demographic information was obtained via a questionnaire developed by the research team with the
54 following items: marital status, partner status, duration of longest relationship, living situation, distance
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3 from parents' home, educational level, number of repeated school years, current employment situation,
4 maintaining livelihood, successful re-integration at school after PHTX. For an overview of items used for
5 the analysis of each developmental domain, see table 1. Additionally, the variables age, sex and date of
6 transplantation were obtained from medical records.
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10 *Social Support Questionnaire- Short Form*

11 The German version of the Social Support Questionnaire-Short Form (Fragebogen zur Sozialen
12 Unterstützung; F-SozU, K-14) was used, which is a 14-item self-report of subjectively perceived or
13 anticipated social support. A total score can be computed, which ranges from 1 to 5 and which was used
14 for the analysis of the domain 'social environment'; see table 1. Psychometric properties are good (33).
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21 *Giessen Complaints Inventory*

22 The German version of the Giessen Complaints Inventory (Gießener Beschwerde-Bogen, GBB) by Brähler
23 and Scheer (1995) was used . The GBB is an instrument for physical complaints frequently used in
24 Germany which measures subjective limitations experienced by patients due to their physical symptoms.
25 The questionnaire comprises 24 items and contains the following subscales: fatigue tendency, gastric
26 complaints, limb pain and heart complaints. Scores per subscale range from 0 to 24. A total score
27 (general discomfort) can be computed, which ranges from 0 to 96 points. The total score was used for
28 the analysis of the domain 'subjective physical well-being'. Psychometric properties are good.
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36 *Kidscreen-27*

37 The KIDSCREEN-27 by Ravens-Sieberer et al. (2005) is a German questionnaire for health-related QoL
38 specifically developed for children. It measures the following five subscales: 'autonomy and parent
39 relations', which we used in the domain 'family', 'perceived social support & peers' and 'school', both of
40 which we used in the domain 'social environment'; 'physical well-being' and 'psychological well-being',
41 which we used in the domains 'subjective physical well-being' and 'subjective psychological well-being'
42 (see table 1). Scores per subscale range from 0 to 100, with a higher score indicating a better QoL. A total
43 score can be computed ranging from 0 to 100 points. Psychometric properties are good (34).
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51 *Short-Form -36-Item Health Survey*

52 The German Version of the Short-Form-36 (SF-36) by Bullinger and Kirchberger (1998) was used, which is
53 a generic health survey comprising 36 items in eight subscales (physical functioning, role functioning
54 physical, bodily pain, general health perceptions, vitality, social functioning, role functioning emotional
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3 and mental health). We subsumed each of the subscales into the domains 'subjective physical well-
4 being' and 'subjective psychological well-being', as appropriate (see table 1). The subscales can be
5 aggregated into two component summary scores representing the physical summary scale and the
6 mental summary scale, both of which we used in the domain 'quality of life' (see table 1). Subscale and
7 summary scores range from 0 to 100, based on transformed z-scores with multiplication of the
8 regression coefficients of the normative sample. A higher score indicates a better QoL. Psychometric
9 properties are good (35).

16 Analysis

17 IBM SPSS Statistics 23 was used for descriptive and inferential statistics. A p-value of ≤ 0.05 was
18 considered statistically significant. Chi-square tests for dichotomous variables univariate analyses of
19 variance were performed for exploratory group comparisons in all developmental domains (for an
20 overview of developmental domains, see table 1). Univariate regressions were conducted for exploratory
21 analyses of predictors of physical and psychological QoL.

27 Results

29 *Sample characteristics*

31 All 38 participants of the PHTX group underwent heart transplantation when they were children, with a
32 mean age at time of transplantation of 10.95 years ($SD=3.7$). The mean age at time of recruitment was
33 22.11 years ($SD=4.7$), ranging from 16 to 35 years. Fifty percent of the patients were male. The mean
34 waiting time for an organ was 0.47 years ($SD=0.5$). Number of years between PHTX and assessment was
35 on average 11.16 years ($SD=5.3$), ranging from 4 to 23 years.

36 In the control group, mean age at assessment was 22.91 years ($SD=1.8$), ranging from 19 to 26 years; 45
37 percent were male.

38 Between groups, there are no significant differences in age ($F(1,45,67) = 1.00, p = 0.285$) or gender ($\chi^2(1,$
39 $N=84) = 1.98, p=0.159$). Regarding the educational level, the control group was significantly more highly
40 educated than the PHTX patients ($F(1,79) = 130.39, p < 0.001$, high school or university in 96% and 8%,
41 respectively). Furthermore, the control group individuals reported being in a partnership more often
42 than the PHTX patients ($\chi^2(1, N=84) = 9.42, p = 0.002$, 65% and 32%, respectively).

52 Family

53 In this domain, we focused on the current living situation, spatial independence and relationship with
54 the parents, with the following results: The living situation differs significantly between the PHTX and
55 control group, $F(1,82) = 4.10, p = 0.046$. Twenty-one of the PHTX patients (55%) lived with their parents,
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while the remaining 45% had moved out. Of those 45%, 18% lived with their partner, 11% lived alone, 11% lived next to their parents in a separate apartment and 5% shared a flat. By contrast, only 22% of the control group lived with their parents, while 78% had moved out, see table 2.

In the subgroup of participants who no longer live with their parents, the distance to the parents' home in km differs significantly between the groups ($F(1,26.0) = 45.57, p < 0.001$). The PHTX stay closer to their parents' house ($M=1.66\text{km}, SD=1.26\text{km}$), while the healthy controls move further away ($M=213.37\text{km}, SD=280.99\text{km}$).

The perceived quality of the relationship with their parents and self-estimated autonomy are reported differently in the two groups ($F(1,57) = 5.72, p = 0.02$), with higher scores reported by the PHTX group than by the control group, indicating higher perceived quality of the relationship and perceived autonomy in the PHTX group, see table 2.

Table 2. Characteristics and metrics of family variables in the PHTX group and control group

Characteristic	assessed by	Value	PHTX (N=38)	Control group (N=46)	p
Living situation	Social demographic questionnaire	With parents	21 (55%)	10 (22%)	0.046
		With partner	7 (18%)	9 (20%)	
		Alone	4 (11%)	10 (21%)	
		Next to parents	4 (11%)	0	
		Flat share	2 (5%)	17 (37%)	
Distance to parents' home in km	Social demographic questionnaire	Mean	1.66	213.37	< 0.001
		SD	1.26	280.99	
Relation to parents and autonomy	KIDSCREEN-27	Mean	59.15	53.49	0.020
		SD	9.27	7.78	

Education and profession

In this domain, we focused on the number of repeated school years, the educational level, employment situation and financial situation. The educational level differs significantly between the two groups ($F(1,79) = 130.4, p < 0.001$): the PHTX patients less often completed high school education than healthy controls (52% and 96%, respectively), fewer of them were currently studying (3% and 62%, respectively) and a smaller percentage achieved an academic degree (5% and 33%, respectively). Three PHTX patients (8%) had dropped out of school, as opposed to no participants from the healthy control group. At school, the PHTX group had to repeat a grade significantly more often than the control group ($\chi^2(1, N=80) = 20.53, p < 0.001$). Ten PHTX patients (26%) repeated one school year and three PHTX patients (8%) repeated two school years, while none of the control group repeated a school year.

The type of the current job also differs between the two groups ($\chi^2 (1, N=79) = 26.36, p < 0.001$), with PHTX patients having part-time jobs less often than the control group (9% and 34%, respectively). The PHTX group's occupations are distributed between jobs in full time (23%), training (11%), apprenticeship (17%), unemployed (23%), retired (11%), half time jobs (3%) or part time jobs (6%) and other (6%). The control group reported the following occupations: full time (5%), training (2%), apprenticeship (40%), unemployed (5%), half time jobs (2%), part time jobs (32%) and other (14%). Finally, sources of financial support differ between the groups ($F(1,78) = 13.44, p < 0.001$): sources of income are more widely distributed in PHTX patients, in comparison with the control group (see table 3). Thirty-four percent of the PHTX group reported being financially independent because of a paid job, as opposed to 64% of the control group. Furthermore, PHTX patients less often receive financial support from their parents than the control group ($\chi^2 (1, N=80) = 11.75, p = 0.001$).

Table 3.

Characteristics and metrics of school, apprenticeship and financial variables in PHTX and control group

characteristics	Value	PHTX (N=38)	control group (N=46)	p
Repeated years at school	Yes	14 (37%)	0	< 0.001
	No	21 (55%)	46	
Number of repeated years at school	0	20 (53%)	46	< 0.001
	1	10 (26%)	0	
	2	3 (8%)	0	
Education level	Still attending school	4 (10%)	0	< 0.001
	No exam	3 (8%)	0	
	School for children with learning difficulties	5 (13%)	0	
	Secondary school level	22 (58%)	1 (2%)	
	A-level	1 (3%)	27 (59%)	
	College	1 (3%)	0	
	University	1 (3%)	15 (33%)	
Current job	Full time	8 (21%)	2 (4%)	< 0.001
	Half time	1 (3%)	1 (2%)	
	Part time	2 (5%)	14 (30%)	
	Training	4 (11%)	1 (2%)	
	Apprenticeship	6 (16%)	18 (39%)	
	Unemployed	8 (21%)	2 (4%)	
	Retired	4 (11%)	0	
	Other	2 (5%)	6 (13%)	
Financial life (multiple choice)	Own money via job	13 (34%)	30 (65%)	<0.001
	Parents/family members	15 (39%)	37 (80%)	
	Dole	5 (13%)	0	
	Pension	8 (21%)	0	
	Welfare	4 (11%)	0	

Others	4 (11%)	8 (17%)
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Partnership

In this domain, we focused on marital status, partner status and the duration of the longest relationship. The marital status differs significantly between the two groups ($\chi^2 (1, N=84) = 14.34, p = 0.002$): 92% of the PHTX patients reported being single, 5% were married and 3% divorced. In comparison, 100% of the control group was single and none were married or divorced. In the subgroup of single participants, 65% of the PHTX patients and 32% of the control group reported having a partner ($\chi^2 (1, N=84) = 9.42, p = 0.002$). The duration of the longest relationship does not differ between groups ($F(1,75) = 1.52, p = 0.222$); see table 4 for an overview.

Table 4.

Characteristics and metrics of partnership in PHTX and control group

Characteristics	PHTX (N=38)	control group (N=46)	p
Marital status			0.002
Single	35 (92%)	46 (100%)	
Divorced	1 (3%)	0	
Married	2 (5%)	0	
Having a partner			0.002
Yes	12 (32%)	30 (65%)	
No	26 (68%)	16 (35%)	
Duration of longest relationship (in months)			0.222
Mean	23.45	31.67	
SD	25.81	29.36	

Social environment

In this domain, we focused on social support in general, social support by peers, feelings about school, re-integration after PHTX, as well as the self-rated social function, with the following results. The PHTX group was asked if re-integration at school after HTX was 'successful or not' (dichotomous variable) as part of the demographic questionnaire. Fifty-eight percent reported the reentry into school as not successful. The total score of the F-SozU differs between the groups ($F(1,44.92) = 23.39, p < 0.001$), with the control group reporting higher perceived social support than the PHTX group. On the KIDSCREEN-27 subscale 'social support by peers', the PHTX group scored lower than the control group ($F(1,75) = 1.52, p$

= 0.22), indicating less perceived support by their peer group. On the SF-36 subscale 'social functioning', the PHTX group also scored lower than healthy controls ($F(1,82) = 6.11, p = 0.015$), indicating poorer social functioning, see table 5.

Table 5.
Social support of PHTX patients and control group

Characteristics	Assessed by	Value	PHTX (N=46)	control group (N=38)	P
Integration in school	Social demographic questionnaire	Successful	16 (42%)		
		Not successful	22 (58%)		
Social support	F-SozU	Mean	4.31	4.77	< 0.001
		SD	0.65	0.28	
Social support by peers	KIDSCREEN-27	Mean	45.5	50.38	0.046
		SD	10.98	7.39	
Feelings about school	KIDSCREEN-27	Mean	50.90	51.19	0.901
		SD	9.47	6.37	
Social functioning	SF-36	Mean	80.59	91.03	0.022
		SD	24.26	13.86	

Subjective well-being and quality of life

In this domain we focused on different aspects of subjective physical well-being (subjective physical complaints, physical functioning, general health, physical limits in everyday functioning, pain and physical well-being), psychological well-being (psychological well-being, vitality, social functioning and emotional limits in everyday functioning) as well as the physical and psychological QoL.

Subjective physical well-being. Subjective physical complaints, as assessed with the GBB total score, do not differ between the two groups ($F(1,83) = 0.78, p = 0.379$). On a subscale level, a significant difference was found on the subscale fatigue tendency ($F(1,83) = 4.39, p = 0.039$), with PHTX patients reporting more fatigue symptoms than the control group ($M=3.0, SD=2.79$ and $M=1.91, SD=1.95$, respectively). No differences were found on the subscales of gastric complaints, limb pain or heart complaints. On the subscale physical well-being of the Kidscreen-27, no significant difference was observed between groups ($F(1,60) = 3.67, p = 0.06$).

Subjective psychological well-being. No significant difference on the Kidscreen-27 subscale 'psychological well-being' was observed between groups ($F(1,60) = 3.93, p = 0.052$).

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3 **QoL.** The PHTX patients reported a lower level of physical QoL based on the physical summary scale of
4 the SF-36 than the control group ($F(1,43.54) = 14.51, p < 0.001$). Also, the PHTX patients scored lower in
5 all physical subscales than the control group (physical functioning: $F(1,82)=21.69, p<0.001$; role physical:
6 $F(1,78)=7.92, p=0.006$; bodily pain: $F(1,82)=6.04, p=0.016$; general health: $F(1,78)=4.9, p=0.03$) (see figure
7 1).

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13 However, the PHTX patients showed no differences in psychological QoL, based on the mental summary
14 scale of the SF-36 ($F(1,76) = 0.15, p = 0.70$). On the subscale-level, only 'social functioning' differed
15 between the groups ($F(1,82) = 6.11, p = 0.015$), with a lower score reported by the PHTX patients (see
16 figure 2).

17 **Predictors of physical and mental quality of life in PHTX patients**

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21 To explore which factors predict QoL (psychological and physical) in PHTX patients, we correlated all
22 variables (from the domains family, education and profession, partnership, social environment and
23 subjective well-being) with the physical and psychological component summary scores of the SF-36 as a
24 first step. Based on significant exploratory correlations, variables were then selected as predictors for
25 each of the two scales. Regression assumptions were checked and met for both regressions. Next, we
26 calculated two stepwise univariate regression models (one for each summary scale of the SF-36).
27 Variables were included stepwise as independent variables in the regression model. In order to avoid
28 overfitting the model, all SF-36 subscales comprising the physical QoL component were excluded from
29 the regression analysis, with the physical summary scale as criterion. All SF-36 subscales comprising
30 psychological QoL were excluded from the analysis, with the mental summary scale as criterion.

31 **Predictors of physical quality of life**

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34 The following predictors were entered in the first regression model, with physical QoL entered as
35 criterion: 1) school re-integration ($r=0.497, p=0.01$); 2) physical complaints ($r=-0.381, p=0.035$); 3) vitality
36 ($r= 0.369, p=0.041$); 4) social support by peers ($r=0.771, p<0.001$); and 5) subjective physical and
37 psychological well-being ($r=0.595, p=0.012$; respectively $r =0.520, p=0.033$,). The analyses revealed that
38 better social support by peers (comprising, for instance, the items 'have you spent time with your
39 friends?' or 'have you and your friends helped each other') predicts a higher physical QoL in PHTX
40 patients, explaining 58.9% of variance ($p=0.001$). See table 6 for the full regression model.

41 **Predictors of psychological QoL**

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44 The following predictors were entered in the second regression model, with psychological QoL as
45 criterion: 1) duration of longest relationship ($r=-0.455, p=0.022$); 2) distance from parents' home ($r=-$

0.443, $p=0.013$); physical complaints ($r=-0.491$, $p=0.005$); 3) role physical ($r=0.498$, $p=0.005$) and 4) subjective psychological well-being ($r=0.683$, $p=0.003$). The analysis revealed two significant predictors: fewer physical complaints and a better role functioning predicted better psychological QoL in PHTX patients, explaining 89.0% of variance ($p<0.001$). See table 6 for the best fitting model.

Table 6.
Stepwise linear univariate regression model: predictors of QoL (n=38)

Criterion	Predictor	<i>B</i>	SE	<i>p</i>	95% C.I. for B	
					Lower	Upper
Physical QoL	Peers (KIDSCREEN-27)	0.77	0.15	0.001*	0.34	0.96
	Constant		6.95	0.01*	5.81	35.64
Mental QoL	Physical Complaints (GGB)	0.40	0.09	0.005*	-0.45	-0.53
	Role Physical (physical subscale SF-36)	0.68	0.07	<0.0001*	0.15	0.45
	Constant		6.5	0.008*	5.53	32.55

Discussion

In this study, we explored developmental tasks of emerging adulthood in a sample of young adults after PHTX in an exploratory manner. The following categories were examined: a) family (current living situation, spatial independence, relationship with the parents) b) education and profession (educational level, repeated school years, employment situation, financial situation) c) partnership (marital status, partner status and duration of longest relationship) and d) social environment (perceived social support in general, by peers, feelings about school, social functioning, and re-integration at school after PHTX). Additionally, subjective physical well-being, subjective psychological well-being and QoL (physical and psychological) were assessed. Finally, we investigated which of the variables from domains a-d, as well as variables from the domains subjective physical and psychological well-being predict self-reported QoL.

In comparison to our control group, PHTX patients more often live with their parents and when they move out, they stay in closer proximity to their parents. We found no differences in the perceived quality of the relationship with the parents.

When it comes to financial independence, the PHTX patients rely less on their family for financial support than the control group. PHTX patients held full-time positions more frequently than the control group, while healthy controls more often chose part time work. Importantly, a significant percentage of PHTX patients had no job and/or received a pension. These findings are similar to those of a recent study by Grady and colleagues, who examined 88 young adults after pediatric heart transplantation in their early

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3 twenties (36). About 50% of the patients reported working for income, compared to 51% in our study
4 (part time work, full time work and apprenticeship taken together). As in our study, PHTX patients more
5 frequently had to repeat at least one school year, probably due to health problems and hospital stays,
6 the choice of full-time work, which might reflect the choice for non-academic career paths, might be
7 related to more academic difficulties related to their disease. Future studies should focus on this issue,
8 systematically investigating academic disadvantages and choices due to underlying disease and the
9 challenges that come with PHTX.
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15 When it comes to partnership, more PHTX patients reported being single than healthy individuals from
16 the control group, even though the groups did not differ in age. However, the duration of the longest
17 relationship did not differ between groups. The results differ somewhat from those of the study by
18 Grady and colleagues (36), in which only 9% of the patients reported having a partner, compared to the
19 32% in our study. This finding might be due to difficulties in initiating partnership, while partnership
20 stability might not be compromised in PHTX patients once they have found a partner. Furthermore, PHTX
21 patients in our sample reported less perceived social support in general and by their peers. Social
22 contacts are of great importance for teenagers and young adults. Facilitating social relationships in order
23 to increase well-being and QoL of this vulnerable group might be an important goal for psychosocial
24 reintegration in patients after PHTX. Future studies should take a closer look at social relationships in this
25 group, focusing on number of social relationships, as well as quality and stability of their social networks.
26 PHTX patients reported a higher fatigue tendency than the control group, while no differences were
27 found in other areas of physical complaints. Symptoms of fatigue might limit PHTX patients' activities in
28 daily life and hinder participation in social life, leisure activities etc. This finding also warrants further
29 investigation.
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33 PHTX patients reported equal psychological well-being to the control group, which is a favorable result.
34 However, they did report lower a physical QoL. In our exploratory regression models, we found that
35 better perceived social support by peers predicts a better physical QoL, with a high proportion of
36 explained variance. While these results further emphasize the importance of peer relations in this age
37 group, the relationship between physical well-being and peer relations should be investigated further.
38 Finally, we found that fewer physical complaints predict a better mental QoL, also with a large
39 proportion of explained variance. In sum, PHTX patients fare well when it comes to their financial
40 autonomy, relationship with their parents and profession, while they only rarely choose an academic
41 career. They report lower social support in general and from peers and have more physical complaints
42 (fatigue tendency), as well as reduced physical QoL, which both seem to be intertwined with social
43 support from peers. While, on average, their mental well-being is comparable to that of the control
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3 group, fewer physical complaints predict higher scores on the mental well-being scale, also pointing to
4 the key role of their physical health for other domains of functioning.
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8 Limitations

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10 Importantly, this study is cross-sectional, exploratory and comprised a small sample of PHTX patients.
11 Accordingly, the results should be cautiously interpreted. Future studies investigating developmental
12 challenges of PHTX patients during emerging adulthood should be longitudinal, in order to shed light on
13 psychosocial adjustment after PHTX across time. Control groups should be carefully matched according
14 to key variables. No correction for multiple testing was applied, as this study is exploratory and
15 hypothesis-generating. Our results need to be interpreted accordingly and replicated in a confirmatory
16 manner.
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31 Conflict of interests

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33 None
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36 Authors' contribution

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38 Maria Sepke and Wolfgang Albert made substantial contributions to the conception and design of the
39 work. Maria Sepke and Hannah Ferentzi contributed to manuscript drafting and editing. Maria Sepke,
40 Hannah Ferentzi, Vera Disselhoff and Wolfgang Albert reviewed the manuscript and made amendments.
41 All authors critically reviewed and approved the final version. All authors agree to be accountable for all
42 aspects of the work.
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48 Data statement section

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50 No additional data available.
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56 profit sectors.
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5 Figure legend

6 Figure 1. Means of z-transformed scores of the SF-36 physical summary scale and all physical subscales
7 raw values 0–100 of PHTX and control group.

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9 Figure 2. Means of z-transformed scores of the SF-36 mental summary scale and all psychological
10 subscales raw values 0–100 of PHTX and control group.
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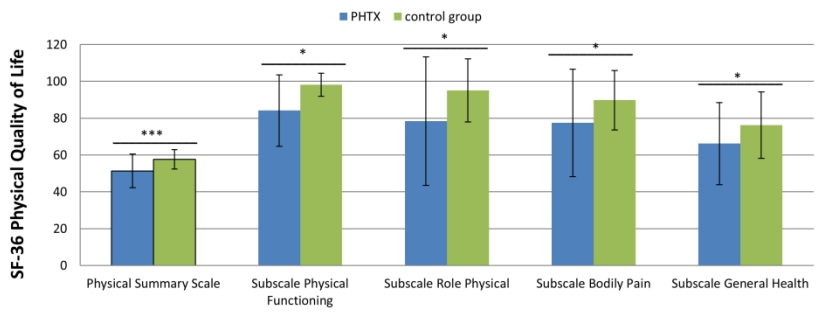


Figure 1. Means of z-transformed scores of the SF-36 physical summary scale and all physical subscales raw values 0–100 of PHTX and control group.

254x190mm (300 x 300 DPI)

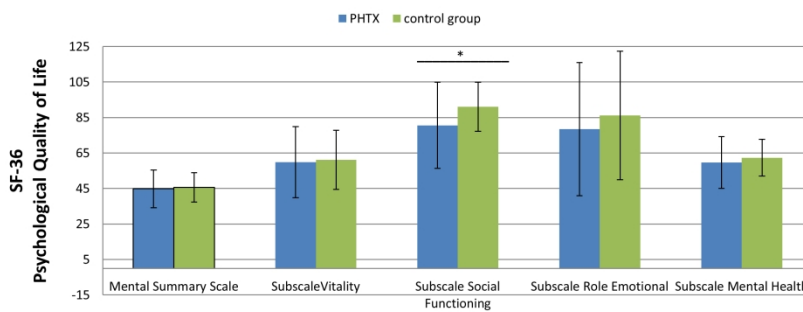


Figure 2. Means of z-transformed scores of the SF-36 mental summary scale and all psychological subscales raw values 0–100 of PHTX and control group.

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Reporting checklist for case-control study.

Based on the STROBE case-control guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE case-control reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandembroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale	5

		for the choice of cases and controls. For matched studies, give matching criteria and the number of controls per case	
	#6b	For matched studies, give matching criteria and the number of controls per case	n/a
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for cases and controls.	6
Bias	#9	Describe any efforts to address potential sources of bias	n/a
Study size	#10	Explain how the study size was arrived at	5
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	6
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	7
	#12b	Describe any methods used to examine subgroups and interactions	7
	#12c	Explain how missing data were addressed	7
	#12d	If applicable, explain how matching of cases and controls was addressed	7
	#12e	Describe any sensitivity analyses	7
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for cases and controls.	7
	#13b	Give reasons for non-participation at each stage	7
	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic,	7

1		clinical, social) and information on exposures and potential	
2		confounders. Give information separately for cases and	
3		controls	
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6		#14b Indicate number of participants with missing data for each	n/a
7		variable of interest	
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9	Outcome data	#15 Report numbers in each exposure category, or summary	7-11
10		measures of exposure. Give information separately for cases	
11		and controls	
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14	Main results	#16a Give unadjusted estimates and, if applicable, confounder-	7-11
15		adjusted estimates and their precision (eg, 95% confidence	
16		interval). Make clear which confounders were adjusted for and	
17		why they were included	
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21		#16b Report category boundaries when continuous variables were	7-11
22		categorized	
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25		#16c If relevant, consider translating estimates of relative risk into	7-11
26		absolute risk for a meaningful time period	
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29	Other analyses	#17 Report other analyses done—e.g., analyses of subgroups and	n/a
30		interactions, and sensitivity analyses	
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33	Key results	#18 Summarise key results with reference to study objectives	11
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35	Limitations	#19 Discuss limitations of the study, taking into account sources of	12
36		potential bias or imprecision. Discuss both direction and	
37		magnitude of any potential bias.	
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40	Interpretation	#20 Give a cautious overall interpretation considering objectives,	11-12
41		limitations, multiplicity of analyses, results from similar studies,	
42		and other relevant evidence.	
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45	Generalisability	#21 Discuss the generalisability (external validity) of the study	12
46		results	
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49	Funding	#22 Give the source of funding and the role of the funders for the	13
50		present study and, if applicable, for the original study on which	
51		the present article is based	
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