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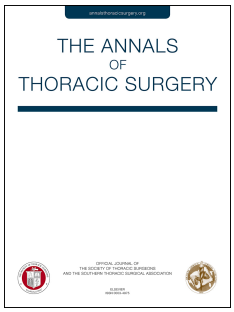

Morbidities following cardiac surgery: impact on children's quality of life and parent mental health

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Morbidities following cardiac surgery: impact on children's quality of life and parent mental health

Running head: Impact of post-operative morbidities

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Abstract

Background: The majority of children now survive cardiac surgery, and the focus of quality improvement initiatives has shifted towards more complex outcome measures. Our aim was to study the impact of early post-operative morbidities on parent-reported patient quality of life and parental anxiety/depression over six months.

Methods: We undertook a prospective case matched cohort study in five UK children's cardiac centers, in which we compared measures of impact for patient categories of 'single morbidity', 'multiple morbidities' and 'extracorporeal life support (ECLS)' with 'no morbidity'. Measures were PedsQL and PHQ-4 at six weeks and six months post-surgery. We modelled the outcomes using mixed effects regression, adjusting for case mix and clustering within centers.

Results: We included 666 patients, operated at a median age of 81 days (IQR 10-325 days). At six weeks follow-up, significant adjusted differences to the reference group with no morbidity were found for total PedsQL scores, which were lower in ECLS ($p=0.01$), multiple morbidities ($p<0.001$) and single morbidity ($p=0.04$); and the proportion of parents with anxiety and depression, which were higher in multiple morbidities ($p=0.04$ and $p=0.01$ respectively). At six months, measures had improved in all morbidity groups: the only significant adjusted difference to the reference group was for physical PedsQL scores in ECLS ($p=0.04$) and multiple morbidities ($p<0.01$).

Conclusions: Patient and parent wellbeing are strongly influenced by post-operative morbidities early after surgery, with improvement by six months. Family psychological support and holistic rehabilitation are vital for children who experience post-operative morbidities.

Early survival after pediatric cardiac surgery is excellent: for instance, 30-day mortality in the UK is <2%.[1] Given this, there is international interest from all stakeholders in studying other (albeit more complex) outcome measures, including rates of specific adverse events, longer-term survival, neurodevelopmental outcomes and health-related quality of life (HRQOL).[2] Such outcomes are inter-related: peri-procedure measures, including hospital length of stay[3] and technical performance score of the operation,[4] have implications for longer term neurodevelopmental function, which is an important determinant of HRQOL.[2] While poorer HRQOL is associated with greater disease complexity[5,6] and medical care utilization, there can be considerable variation within specific diagnostic groups, suggesting other factors are also important.[2] Specific individual post-operative adverse events have links with longer term neurodevelopmental function (seizure, acute neurological event, cardiac arrest),[7,8] hence post-operative complications have become an important focus of clinician collaboratives seeking to leverage further improvements in outcome. For parents, the traumatic nature of cardiac surgery in their children and the subsequent stay in intensive care has been well described,[9] as has the influence of parent functioning on child psychosocial outcomes.[10]

Our qualitative research showed that clinicians and parents hold differing views about which specific post-operative events should be counted as an adverse early outcome of pediatric cardiac surgery.[11,12,] Therefore, we used the term *morbidity*, a state of health generally viewed as bad for you, to label the range of adverse early outcomes (excluding death). We recognized that not all such adverse early outcomes are directly caused by the surgery, although they do arise as a direct consequence of children undergoing cardiac surgery. Our overarching study aim was to *evaluate the important early morbidities*

following pediatric cardiac surgery, in terms of their incidence and impact on patients, families and the National Health Service. We have previously published[13-15] the selection[15] and definition[13] of nine key surgical morbidities (acute neurological event, renal replacement therapy, necrotizing enterocolitis (NEC), major adverse events, extracorporeal life support (ECLS), post-surgical infection, prolonged pleural effusion or chylothorax, unplanned re-intervention, and feeding problems – summarized in Table 1, supplementary material) and the incidence of these in a UK population[14] but the impact of these on patient and parent psychosocial outcomes has not been previously addressed. Our aim in this phase of the study, therefore, was to *evaluate the impact of the selected morbidities on parent-reported patient HRQOL and parent anxiety/depression up to six months after surgery.* We hypothesized that ECLS and multiple morbidities (excluding ECLS) would have a greater impact on parent-reported HRQOL and parent anxiety/depression than single morbidities or no morbidity.

Patients and Methods

The study received ethical approval from London City Road Research Ethics Committee (14-LO-1442) and all participants provided written consent.

Our study design was a prospective, multi-center case matched cohort study in which HRQOL was prospectively assessed at six weeks and six months after cardiac surgery.

Patients were eligible to participate if they were <17 years of age and had pediatric cardiac surgery in one of five participating centers in the UK either electively or as an emergency,

were UK residents, and their family were able to speak and understand English to a reasonable standard.

From the eligible pediatric cardiac surgery patients meeting criteria, all patients with at least one of the selected morbidities[15] were approached for participation as a *morbidity case*. A subset of patients with none of the selected morbidities were approached for participation as *morbidity-free controls*.

As described previously,[12] within each center we aimed to match each *morbidity case* with the next patient who did not have a morbidity (*a morbidity-free control*) using the following criteria:

1. Age within 3 months for children <12 months old; within 12 months for children aged 1-5 years and within 2 years for children aged >5 years)
2. Single or biventricular condition

Baseline clinical[16,17] and demographic[18] data previously linked to early mortality and/or HRQOL were collected details of which are provided in supplementary material Tables 2, 3 and 4. Further detail about recruitment and baseline data collection processes are provided in Table 5 (supplementary material).

Follow-up data

Outcome measure data were collected with families at six weeks and six months after surgery excepting when the child had died. If a child was still in hospital at follow-up, data were collected wherever possible. Data were collected either face-to-face, by telephone or electronically, depending on parental preference.

Perceived HRQOL was assessed with the parent-completed PedsQL™ Generic and Infant scales,[19,20] which include parent-proxy assessment for children aged 1 month-18 years. A total score, physical health summary score and psychosocial summary score were computed (range of 0-100).

The PHQ-4[21] was used to assess parental anxiety and depression. This ultra-short screening measure comprises four questions, two each for anxiety and depression. Parent PHQ-4 scores were dichotomized to indicate the potential presence or absence of anxiety and depression.

The primary measure of impact was the PedsQL4.0 Total Score. A clinically meaningful difference in HRQOL scores between pairs corresponds to a mean difference of at least 0.5 standard deviations;[22] to detect such a difference between cases and controls with 80% power and 5% significance would require 32 matched pairs of patients with/without morbidity. Allowing for an attrition rate of 10%, we aimed to recruit 36 matched pairs for each selected morbidity.

Data Analysis

In view of the small numbers in selected individual morbidity categories and our hypothesis related to ECLS and multiple morbidities, we categorized morbidities as: 'single morbidity' (one of the selected morbidities excluding ECLS), 'multiple morbidity' (more than one selected morbidity excluding ECLS) and 'ECLS' (those on ECLS even if they had other morbidities).

PedsQL scores and categorized PHQ-4 scores were summarized using means (SD) and frequencies (proportions) as appropriate for each morbidity group at both six weeks and six months. We fitted separate mixed-effects regression models, for all outcomes at both time points and included the four-category morbidity factor and pre-specified covariates (age, weight, cardiac diagnosis category, functionally univentricular heart, specific procedure type, bypass time, acquired comorbidity, congenital comorbidity excluding Downs syndrome, additional cardiac risk factors and severity of illness). The primary analysis considered all patients, and all models included a random factor for patient, nested within matched pairs, to account for the correlation between matched pairs.

Using the 'no morbidity' group as the reference category, the absolute differences in means and 95% confidence intervals are presented for the three morbidity groups, for each of the continuous outcomes. Odds ratios are presented along with 95% confidence intervals for the categorical outcomes.

Multiple imputation using chained equations was used to account for missing data in all analyses.

All analyses were performed in Stata v14.

Results

We recruited 340 patients with at least one morbidity (60% of eligible patients), and 326 controls with none of the selected morbidities, of whom 558 were case-control matched.

Case-mix

The number and proportion of patients with pre-defined baseline characteristics are shown in Table 3 (supplementary material), in the study population overall and by the morbidity

groups. The study population was relatively young and complex: at the time of operation 410 (76.6%) were <12 months old; 121 (18%) had congenital comorbidities other than Down syndrome, and 135 (20%) had functionally univentricular hearts. The majority lived in two-parent families (n=523; 93.7%) with an annual income of >£25,000 per annum (median for UK) (n=361; 63.3%) and were of white ethnicity (n=501; 83%).

Loss to follow-up

At six weeks, 19 (3%) patients had died and 70/647 (11%) were still in hospital. At six months, 39 (6%) had died and 5/627 were in hospital. PedsQL total scores were available for 477 (74% of surviving patients) at six weeks and 407 (65%) at six months. PHQ-4 data were available for 482 (74%) at six weeks and 394 (63%) at six months. Compared with those with non-missing data, the proportion with baseline severity of illness risk factors and acquired cardiac risk factors was higher ($p<.01$) in those with missing data at six weeks but not at six months. There were no differences in other baseline factors or in the proportion with a morbidity, between patients with and without missing follow-up information.

Morbidities

Figures 1-4 indicate the number of patients with each morbidity type and depict PedsQL physical and psychosocial summary scores and proportions of parents with anxiety or depression according to the presence of no selected morbidity, each individual single morbidity, multiple morbidities and ECLS.

Analyses of morbidity impact

Table 1 shows mean PedsQL scores at the two follow-up time points by the four morbidity groups and the adjusted comparisons of these scores based on single morbidities, ECLS and multiple morbidities, to the reference category of no morbidities. After adjusting for covariates, at six weeks physical HRQOL was worse for single morbidities, ECLS and multiple morbidities ($p<0.01$). In contrast, for psychosocial HRQOL we observed no difference for single morbidities and ECLS, but there was a reduction in adjusted psychosocial HRQOL with multiple morbidities ($p=0.03$). By six months, the differences in adjusted PedsQL scores by the morbidity groups had narrowed considerably and the only residual significant adjusted differences were for physical HRQOL in ECLS ($p=0.04$) and multiple morbidities ($p<0.01$).

Table 2 shows the PHQ-4 outcomes and adjusted comparisons based on morbidity group. At six weeks there was a higher adjusted rate of potential anxiety and depression in the multiple morbidity group ($p=0.04$ and $p=0.01$ respectively) referenced to the no morbidity group. For the single morbidities and ECLS groups at six weeks and for all three morbidity groups at six months, there were no significant differences in the rates of either anxiety or depression in comparison to the no morbidity group.

Outcome scores did not differ at six weeks between those who did and did not have six month data.

Comment

Our prospective case-matched multi-center cohort study enabled us to explore measures of early post-operative morbidity impact in a large group of vulnerable children and their families. HRQOL was significantly worse at six weeks after surgery based on the presence of

morbidity, after adjustment for case mix and family factors. This reduction in HRQOL was more pronounced for children who had multiple morbidities and ECLS than for single morbidities, supporting our hypothesis, and involved marked impairments in physical HRQOL. Encouragingly, HRQOL improved between six weeks and six months.

Implications of our study

Recently, registries and collaboratives have supplemented mortality data with reports of post-operative complications across multiple centers.[23] These initiatives have been complemented by single center and cross-sectional studies of HRQOL in survivors of paediatric cardiac surgery,[24] showing poorer HRQOL in those with more complex disease,[2,5,6] however prospective multi-center studies of post-operative HRQOL related to morbidity are lacking. A strength of our study was the heterogeneous sample and prospective multi-center data collection, increasing the potential for our findings to be generalizable. Nonetheless, generalizability will be influenced by the sample characteristics: in previous retrospective studies, complex CHD has been linked to worse HRQOL and more privileged sociodemographic characteristics have been linked to better HRQOL.[25,26]

Neurological events and neurodevelopmental surveillance

In earlier stages of our research, parents and other stakeholders reported that neurological events were the morbidity they were most concerned about.[13] The rate of acute neurological event was very low and did not enable us to look at the impact of it in isolation, however there were higher rates of scores suggestive of potential anxiety in this group at six months. There is a wealth of data on neurodevelopmental sequelae of cardiac surgery in the longer term[27,28] but our measurement of 'acute neurological events' during the

perioperative period was not able to capture the extent of this. Our findings nonetheless support the recommendation[28] of regular neurodevelopmental surveillance after hospital discharge.

Rehabilitation after heart surgery

Physical HRQOL was most impacted, and this may relate to the physical demands and effects of living with a complex heart defect and is consistent with other studies.[6,18,26] As might be expected, children's physical HRQOL improved over time as they recovered after surgery. There is a growing interest in the area of rehabilitation following critical illness and surgery in children[29] and our study supports this for pediatric cardiac surgery.

Psychological support

A high proportion of parents whose children had morbidity had scores suggestive of anxiety, and to a lesser extent depression, at six weeks, supporting previous findings.[9] Of interest, depression scores in the ECLS and multi-morbidity groups increased between six weeks and six months, likely related to the residual effects of these morbidities. There have been relatively few trials of psychosocial interventions for parents of children with CHD and provision of psychological support varies. Although all centers in the UK offer psychological support, it is unlikely that the needs of all parents are recognised and met. The use of screening tools such as the PHQ-4 might facilitate early, targeted referral.

Feeding problems

"Feeding problems" was a common morbidity, identified by our lay advisers as particularly important.[13] The negative impact on parents and the challenges of feeding babies with CHD

are widely reported in the literature,[30] with some parents reporting that feeding problems after discharge overshadow any other cardiac concerns.[31] Children requiring tube feeding are also more likely to experience neurodevelopmental delay,[32] which may also contribute to parental anxiety. Our results support these findings as indicated by the higher anxiety scores in this group at six months.

Study limitations

Whilst we recruited 60% of eligible patients and had a high response rate, those who died or who were sickest could not participate thus introducing a source of bias. The measures we used required at least one parent to speak English, which might have contributed to the relatively high proportion of White British families and also introduces a further source of bias. We found lower than anticipated incidence of some specific morbidities, and this prevented us from exploring links between single morbidities and outcome. The prospective, observational nature of the study and its design limits the interpretation of our findings to inference rather than direct attribution of cause. A further potential limitation is the use of a generic measure (PedsQL) which is less able to discriminate between severity levels of a condition than a disease-specific measure. Finally, all outcome data were provided by parents because the majority of children (92.4%) were under 5 years of age.

Conclusions

Post-operative morbidities significantly impact patient and family wellbeing early after pediatric cardiac surgery, improving over 6 months. Family psychological support and efforts at holistic rehabilitation are important for those with post-operative morbidities. Patients and families should be appropriately prepared before surgery for the risk and consequences

of morbidities, since normalizing experiences and managing expectations may help to reduce anxiety and depression. In addition, investigation is warranted to understand and learn from families who report coping well through their cardiac surgery pathway and hence aid the design of effective psychosocial support strategies. Finally ensuring that non-English speaking families are able to access appropriate information and support needs to be addressed. Further longitudinal research now needs to be undertaken to identify the longer-term impacts of surgical morbidities, monitor how HRQOL and parental anxiety/depression change over time and to inform the implementation of appropriate screening and intervention programs for at-risk groups.

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Table 1: Mean (SD) PedsQL scores at follow-up points by the four morbidity groups and fully adjusted comparison of these scores by morbidity groups

PedsQL scale: **6 weeks**	No Morbidity (n=241) Mean score (SD)	Single Morbidity (n=145) Mean score (SD)	ECLS Morbidity (n=13) Mean score (SD)	Multi Morbidity (n=78) Mean score (SD)		Single v None Difference in means (95% CI) P value	ECLS v None Difference in means (95% CI) P value	Multi v None Difference in means (95% CI) P value
Physical	79.0 (16.2)	72.4 (21.1)	50.4 (23.2)	66.1 (20.9)		-6.2 (-10.3, -2.1) < 0.01	-20.2 (-30.9, -9.5) < 0.001	-12.2 (-17.1, -7.3) < 0.001
Psychosocial	79.4 (14.7)	76.8 (17.3)	65.6 (24.1)	73.5 (20.9)		-1.7 (-5.4, 2.0) 0.37	-6.1 (-16.1, 3.8) 0.23	-5.1 (-9.6, -0.5) 0.03
Total score	79.3 (13.8)	74.5 (18.3)	59.4 (22.0)	69.6 (19.3)		-3.9 (-7.4, 0.3) 0.04	-12.4 (-21.7, -3.2) 0.01	-8.3 (-12.6, -4.0) < 0.001
PedsQL scale: **6 months**	No Morbidity (n=209) Mean score (SD)	Single Morbidity (n=125) Mean score (SD)	ECLS Morbidity (n=11) Mean score (SD)	Multi Morbidity (n=62) Mean score (SD)		Single v None Difference in means (95% CI) P value	ECLS v None Difference in means (95% CI) P value	Multi v None Difference in means (95% CI) P value

Physical	82.3 (16.6)	79.2 (16.8)	68.4 (28.0)	72.6 (19.6)		-2.3 (-6.5, 1.8) 0.27	-12.4 (-23.9, 0.9) 0.04	-7.0 (-12.3, -1.6) < 0.01
Psychosocial	78.0 (14.7)	76.9 (14.1)	78.9 (18.8)	74.9 (17.4)		-0.3 (-4.0, 3.4) 0.88	-3.3 (-13.6, 6.9) 0.52	-1.4 (-5.9, 3.1) 0.54
Total score	79.8 (13.9)	78.1 (14.0)	74.6 (21.4)	74.0 (15.8)		-1.1 (-4.7, 2.4) 0.53	-7.4 (-17.1, 2.4) 0.14	-3.7 (-8.1, -0.7) 0.1

Table 2: Number (%) of parents with anxiety and depression by four morbidity groups at follow-up time points, and fully adjusted odds ratio of anxiety and depression by morbidity groups at the two time points

	No Morbidity Number (%)	Single Morbidity Number (%)	ECLS Morbidity Number (%)	Multi Morbidity Number (%)		Single v None Odds ratio (95% CI) P value	ECLS v None Odds ratio (95% CI) P value	Multi v None Odds ratio (95% CI) P value
Anxiety	55 (23.7)	51 (33.8)	9 (56.3)	32 (38.6)		1.62	3.09	1.89
No Anxiety	177 (76.3)	100 (66.2)	7 (43.7)	51 (61.4)		(1.00, 2.62)	(0.90, 10.61)	(1.04, 3.43)
(At 6 weeks)						0.05	0.07	0.04
Depression	26 (11.2)	27 (18.0)	6 (37.5)	22 (26.5)		1.62	3.18	2.44
No Depression	206 (88.8)	123 (82.0)	10 (62.5)	61 (73.5)		(0.88, 2.97)	(0.90, 11.24)	(1.21, 4.92)
(At 6 weeks)						0.12	0.07	0.01
Anxiety	23 (11.5)	19 (15.5)	3 (27.3)	12 (19.7)		1.25	1.84	1.53
No Anxiety	177 (88.5)	104 (84.5)	8 (72.7)	49 (80.3)		(0.63, 2.45)	(0.43, 7.90)	(0.72, 3.21)
(At 6 months)						0.52	0.41	0.27
Depression	15 (7.5)	9 (7.4)	2 (18.2)	12 (19.7)		1.16	2.88	2.04

No Depression **(At 6 months)**	185 (92.5)	113 (92.6)	9 (81.8)	49 (80.3)		(0.51, 2.64) 0.73	(0.39, 21.16) 0.30	(0.84, 4.97) 0.11

Figure Legends

Figures 1 and 2: PedsQL physical and psychosocial summary scores by morbidity type at 6 weeks and 6 months after primary operation. The boxplots show the PedsQL summary score, for no selected morbidities (blue), for each selected morbidity in isolation and multiple morbidities (red for 6 weeks post-operation and orange for 6 months post-operation). The middle heavy bar represents the median, the box represents the IQR 25th (Q1) to 75th centiles (Q3), and the outer lines ending in a bar represent the threshold for lowest and highest deciles.

Figures 3 and 4: Percentage of parents with potential anxiety or depression, determined by the PHQ-4 at 6 weeks and 6 months after primary operation. Percentages are shown for no selected morbidities (blue), for each selected morbidity in isolation and multiple morbidities (red for 6 weeks post-operation and orange for 6 months post-operation), with 95% confidence intervals.