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Health-related quality of life of pediatric intensive care survivors

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Abstract

Objective: To assess the health-related quality of life (HRQoL) of children surviving to pediatric intensive care discharge.

Methods: A prospective evaluation of HRQoL at admission and 6 months later was carried out with children aged 6 years or more, admitted to three tertiary pediatric intensive care units (PICUs) from May 2002 to June 2004. HRQoL was measured with the Health Utilities Index Mark 3 (HUI3) questionnaire, administered to a child's proxy.

Results: From the 517 eligible admissions, 44 children died in the PICU (8.5%) and 320 cases were evaluated at admission; among those, follow-up data were available in 252 cases. There were no statistically significant differences between preadmission and follow-up HUI3 global scores (medians [interquartile range] of 0.86 [0.42-1.00] and 0.83 [0.45-1.00]; p = 0.674, respectively). At the individual level, 21% of children had their HRQoL unchanged, improvement was seen in 40% and deterioration in 38% of the cases. Severe disability before admission (HUI3 global score < 0.70) was present in 36% of the cases, with improvement at the 6-month follow-up in 60% of them. Among those with deterioration of HRQoL at follow-up, 45% were trauma victims.

Conclusions: Although the HRQoL was globally similar in both evaluations, several differences were found at the individual level. Children with low preadmission HRQoL (severe disability) may benefit from pediatric intensive care, since many of these children improved their HRQoL compared to preadmission status.

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Introduction

During the last decades, the progressive reduction in pediatric intensive care unit (PICU) mortality rates and the recognition that some children were surviving with poor functional status suggested the need of other quality of care indicators in addition to the traditional PICU outcomes (such as mortality, length of stay, or use of mechanical ventilation), and generated a movement towards the evaluation of PICU survivors regarding their morbidity and physical and psychological sequelae, as well as the evaluation of their health-related quality of life (HRQoL).[1-5]

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Additionally, many children admitted to the PICU have chronic disease, with functional disability and impaired HRQoL.[6] Thus, it is extremely important to evaluate the true benefits of intensive and invasive care in these children by assessing the changes in their health status before and after PICU care. Several studies evaluated the HRQoL of children admitted to the PICU[3,5-14] but few provided a prospective evaluation of changes after PICU discharge.[7,10]

In this study, we aimed to assess the HRQoL status of children admitted to three PICUs before admission and 6 months later, and to compute the changes in the HRQoL between these two moments. To our knowledge, this is the first study in the PICU setting that applies the Health Utilities Index Mark 3 (HUI3) questionnaire[15] and performs a longitudinal evaluation of HRQoL changes in children admitted to the PICU.

Methods

Health Utilities Index

HRQoL was measured using the Health Utilities Index (HUI) instrument. The HUI includes three different questionnaires: the HUI Mark 1,[16,17] the HUI Mark 2 (HUI2),[18,19] and the HUI3,[15] developed to address some limitations of the previous versions and to be able to measure HRQoL in adults and children above 5 years old.

The version of the questionnaire used in this study is the HUI23P1P.40Q, referred as HUI3 hereafter. It was administered by interview (direct or telephone) with children's proxies, referring to the child's health status with a recall period of 1 week ("during the last week").

HUI3 is a multi-attribute generic questionnaire, based on preferences from general population, about eight different attributes - vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. Each attribute has five or six different levels (depending on the attribute), from perfect function to the most abnormal function. The health status of each child can also be described as a vector of responses to the eight attributes ($X_1X_2X_3X_4X_5X_6X_7X_8$), where X_i represents the level (from 1 to 5 or 6) in each attribute. For example, the sequence 11111111 indicates a child with perfect function in all eight attributes. Answers like "Don't know" or "Refuse to answer" are allowed, but in these cases the attribute being evaluated, as well as the global score, cannot be computed; for this reason, the number of cases varies slightly across attributes and for the global score.

The HUI3 global score is obtained by a multiplicative formula of the values for each attribute evaluated [global score = $1.371 * (X_1*X_2*X_3*X_4*X_5*X_6*X_7*X_8) - 0.371$], ranging from -0.36 to 1.00. This scale has anchors at zero and one, corresponding to death and perfect health, respectively; negative values are interpreted in the literature as health status theoretically "worse than death."[20]

More detailed information about the HUI system and its psychometric properties have been published elsewhere.[15,20-24]

Study participants

Demographic and clinical data were collected prospectively from May 2002 to June 2004 for all children admitted to three PICUs located at tertiary hospitals.

The HUI3 was applied to proxies (parents or guardians) of all children aged between 6 and 18 years old, at two different time points: (1) at PICU admission, referring to the health status of the child in the "last week" (i.e., 7 days before admission) and (2) 6 months after admission, referring to the child's health status in the week previous to the interview. The first questionnaire was applied by direct interview with one of the physicians involved in the study, as early as possible after the admission. The second questionnaire was applied by telephone interview conducted by one of the two research assistants, who were not members of the clinical team and were blinded to the initial clinical condition of the child.

Children were excluded from the study at admission if they were readmitted to the PICU within 30 days after admission (only the first admission was analyzed) or if they died in the PICU. Children were excluded at follow-up in case of wrong contact information and if no answer was obtained after five phone call attempts during a 1-week period.

Statistical analysis

The change in HRQoL was defined as a variation greater than 0.05 in the global score, between pre and post PICU admission. If the change in HRQoL between the 6-month follow-up and admission was higher than 0.05, it was considered an improvement in HRQoL; if it was inferior to -0.05, it was considered a deterioration in HRQoL; and if it was between -0.05 and 0.05, it was classified as "no change" in HRQoL.

HUI3 global score was analyzed in relation to demographic and clinical variables and was also recoded into three disability categories, as suggested by David Feeny[24]: no disability (1.00), mild/moderate disability (0.70-0.99), and severe disability (< 0.70).

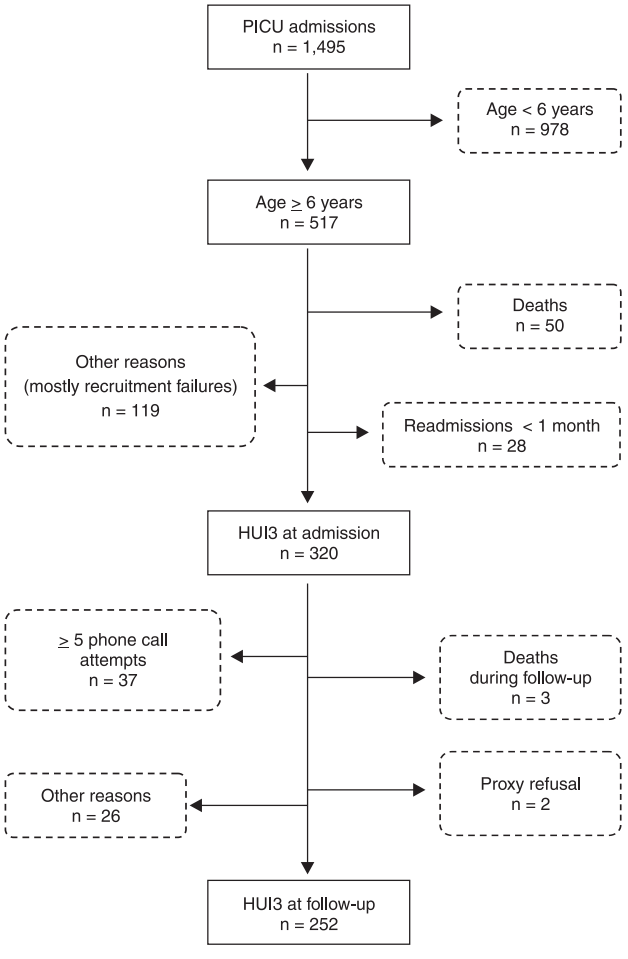
Chi-square and Fisher's tests were used to study the association between categorical variables. The comparison of health status before and after admission was performed with the McNemar and Wilcoxon tests, for categorical and continuous scales respectively. Statistical significance was considered at $p < 0.05$ and the analysis was performed using the software SPSS® v.17.0.

The Ethics Committee of each of the participating hospitals approved the study. Previous informed consent was obtained from all children's proxies.

Results

A total of 1,495 children were admitted to the three PICUs during the study period. After protocol exclusions, a total of 320 cases were evaluated at admission (62% of the 517 eligible cases and 21% of total admissions) and the follow-up interview was obtained in 252 cases (79% follow-up rate) (Figure 1).

The PICU mortality rate was 8.5% (44/517) within the eligible cases. Six other children died in hospital after PICU discharge (1.2%). Only two proxies refused to participate in the study (2/322; 0.6%). The main cause of study exclusion at admission to the PICU was unavailability of an investigator to contact and interview the proxies. At the follow-up, two other proxies (2/257) refused to be interviewed despite initial agreement, and three children died during this time, accounting for 1.2% of cases (3/257). Most of the other exclusions at follow-up were due to impossibility to establish contact within the five phone calls attempts.



HUI3 = Health Utility Index Mark 3 questionnaire;
PICU = pediatric intensive care unit.

Figure 1 - Flow diagram of exclusions from the study at admission to the PICU and at follow-up

Demographic and clinical data from our population are presented in Table 1.

We found significant differences between children with and without follow-up regarding type of admission, Glasgow Coma Scale, and length of stay.

HUI3 attributes' distribution, at admission and at follow-up, showed that all worst levels of function were represented with at least two cases. Of the 45 possible different attribute levels, only four of them had no cases, with three of these levels belonging to the hearing attribute. Attributes with more abnormalities were emotion, cognition, and pain, both at admission and follow-up.

From the 320 cases, only 294 had complete questionnaires at admission. The health status of these 294 cases can be described using 120 different vectors (0.41 vector/case). The ratio between the number of different vectors and the number of cases provides a measure of heterogeneity in the health status. After exclusion of the 92 cases with the vector representing perfect health ([11111111]), this ratio increased to 0.59 vector/case. At follow-up, the 219 fully completed questionnaires resulted in 101 vectors (0.46 vectors/case) and in 0.65 vector/case after exclusion of the 65 cases with the [11111111] vector. Analysis of the resulting 210 paired vectors revealed that "no change" occurred in 31 cases (15%), with the remaining 85% of children having changes in at least one of the HUI3 attributes. From the 31 cases with no change, the majority (84%) were children with perfect health status at both moments. In the paired analysis, deterioration was observed in 62% (43/69 cases) of children with perfect health before PICU admission. This number is counter-balanced by the 36 cases with preadmission morbidity but perfect health status at follow-up (representing 58% of the total 62 cases with perfect health at follow-up).

The number of affected attributes in each individual case showed that the majority of cases (54 and 56% at admission and follow-up, respectively) had none or at most one attribute affected.

The medians (interquartile range) of the HUI3 global score were 0.86 (0.42-1.00) and 0.83 (0.45-1.00) for admission and follow-up, respectively; differences were not statistically significant ($p = 0.674$). Negative values of the HUI3 global score were found in 9 and 7% of cases at admission and follow-up, respectively. The number of children with improvement in the HUI3 global score was similar to those who had some deterioration in their health status (38% vs. 40%, $p = 0.756$). However, there were significant differences regarding the individual attributes (Table 2).

We observed significantly more deterioration than improvement for vision (10% vs. 2%, $p = 0.002$), speech (11% vs. 2%, $p < 0.001$) and cognition (33% vs. 14%, $p < 0.001$). On the other side, although there was

significantly more improvement (32%) in the attribute pain (p = 0.004), a considerable number of children (19%) experienced some deterioration in this attribute.

Nearly half of the children with non-elective admission had deterioration in their health status, while 72% of elective admissions had no changes or had an improvement (p = 0.008). Not surprisingly, 75% of trauma victims had a decrease in their health status (Table 3). These patients accounted for 47% (40/85) of the cases with deterioration of HRQoL.

Table 1 - Demographic and clinical characteristics of the studied children (n = 320) according to the completion (or not) of the HUI3 questionnaire at the 6-month follow-up

	HUI3 at admission (n = 320)		HUI3 at follow-up (n = 252)		No HUI3 at follow-up (n = 68)		
	n	(%)	n	(%)	n	(%)	p*
PICU							0.018
x	120	(38)	97	(38)	23	(34)	
y	85	(27)	58	(23)	27	(40)	
z	115	(36)	97	(38)	18	(26)	
Gender							0.973
Female	150	(47)	118	(47)	32	(47)	
Male	170	(53)	134	(53)	36	(53)	
Admission year							0.923
2002	86	(27)	69	(27)	17	(25)	
2003	157	(49)	123	(49)	34	(50)	
2004	77	(24)	60	(24)	17	(25)	
Admission type							0.003
Elective	125	(39)	109	(43)	16	(24)	
Non-elective	195	(61)	143	(57)	52	(76)	
Mechanical ventilation							0.457
Yes	185	(58)	143	(57)	42	(62)	
No	135	(42)	109	(43)	26	(38)	
PRISM-III							0.652
≤ 1%	175	(55)	138	(55)	37	(54)	
]1-5%]	93	(29)	76	(30)	17	(25)	
]5-15%]	33	(10)	24	(10)	9	(13)	
]15-30%]	7	(2)	6	(2)	1	(2)	
> 30%	12	(4)	8	(3)	4	(6)	
Glasgow Coma Scale†							0.015
≤ 8	53	(22)	35	(18)	18	(34)	
> 8	190	(78)	155	(82)	35	(66)	
Length of stay (days)							0.018
< 1	67	(21)	51	(20)	16	(24)	
[1-4[	146	(46)	124	(49)	22	(32)	
[4-7[	49	(15)	37	(15)	12	(18)	
[7-14[	31	(10)	18	(7)	13	(19)	
≥ 14	27	(8)	22	(9)	5	(7)	
Diagnostic group							0.065
Post-operative elective	112	(35)	97	(38)	15	(22)	
Respiratory	21	(7)	15	(6)	6	(9)	
Sepsis/septic shock	19	(6)	16	(6)	3	(4)	
Trauma	80	(25)	62	(25)	18	(26)	
Other	88	(28)	62	(25)	26	(38)	

HUI3 = Health Utility Index Mark 3 questionnaire; PICU = pediatric intensive care unit; PRISM = pediatric risk of mortality.
* Pearson chi-square test.
† Collected only in cases with known or suspected acute neurologic changes.

Table 2 - Changes in HRQoL status between preadmission and follow-up: absolute numbers and relative frequencies (%) for attributes and HUI3 global score

	Deterioration		No change		Improvement		
	n	(%)	n	(%)	n	(%)	p*
Vision	23	(10)	207	(88)	6	(2)	0.002
Hearing	6	(3)	229	(97)	1	(0)	0.125
Speech	27	(11)	216	(87)	6	(2)	< 0.001
Ambulation	17	(7)	208	(84)	23	(9)	0.430
Dexterity	23	(9)	215	(86)	12	(5)	0.090
Emotion	63	(26)	122	(50)	57	(24)	0.648
Cognition	80	(33)	130	(53)	33	(14)	< 0.001
Pain	47	(19)	121	(49)	80	(32)	0.004
HUI3 global score	85	(40)	45	(21)	80	(38)	0.756

HRQoL = health-related quality of life; HUI3 = Health Utility Index Mark 3 questionnaire.
* McNemar test: comparison between the proportions of patients that improved vs. patients that deteriorated.

Table 3 - Absolute numbers and relative frequencies (%) of the change between preadmission and follow-up HUI3 global scores, according to some clinical variables

	HUI3 global score						
	Deterioration (n = 85)		No change (n = 45)		Improvement (n =80)		
	n	(%)	n	(%)	n	(%)	p*
Children health status at admission†							< 0.001
Excellent/very good/good	66	(52)	33	(26)	29	(23)	
Fair/poor	18	(22)	12	(15)	51	(63)	
Admission type							0.008
Elective	24	(28)	23	(27)	39	(45)	
Non-elective	61	(49)	22	(18)	41	(33)	
Main diagnostic group							< 0.001
Elective post-operative	23	(30)	24	(32)	29	(38)	
Trauma	40	(75)	9	(17)	4	(8)	
Other	22	(27)	12	(15)	47	(58)	
Mechanical ventilation							< 0.001
Yes	55	(47)	29	(25)	34	(29)	
No	30	(33)	16	(17)	46	(50)	

HUI3 = Health Utility Index Mark 3 questionnaire.
* Pearson chi-square test.
† One proxy refused to answer this question.

Frequency distribution of HUI3 global score recoded into three disability categories showed that severe disability at admission (HUI3 global score < 0.70) was present in 36% of the paired cases, among which 60% had an improvement, with 25% of those returning to a perfect HRQoL status. Mild/moderate preadmission disability was present in 31% of cases, and 33% had no disability (of these, 45% had some disability at follow-up).

Discussion

In this study, we characterized the magnitude of the HRQoL phenomena in the PICU setting in order to promote more objective and fine-tuned "clinical impressions" on the HRQoL of PICU patients.

HUI3 global score has a clear skewed distribution, with a high concentration of patients near the upper limit of the

scale (1.00 - perfect health state), both before and 6 months after admission to the PICU. However, 9 and 7% of cases, at preadmission and follow-up respectively, had negative scores, representing a small but important proportion of PICU patients with severe impairment.

The most affected attributes, both before admission and at follow-up, were emotion, cognition and pain, which coincides with other studies involving populations with severe health problems, such as oncologic children.[25] Despite significant changes in half of the attributes, the HUI3 global score had no significant differences between the two evaluations.

Distribution of cases within each attribute is also skewed to the upper value limit at admission and follow-up. However, there were cases represented in most levels of all attributes. Of the 45 different possible levels for the HUI3 attribute classification, only four levels had no case represented (three at admission and one at follow-up) but, in a joint evaluation of both questionnaires, all the 45 levels were represented, which indicates a good discriminant validity of the HUI3 questionnaire and also reflects the high heterogeneity and morbidity of the children cared in our PICUs.

HRQoL global score remained unchanged in only 21% of cases, although much higher percentages of "no change" (from 49% in pain up to 97% in hearing) were observed in the individual attributes. This difference can be explained by the multidimensional and multiplicative formula for calculation of the HUI3 global score, which accumulates any difference in the attributes. Deterioration of HRQoL occurred in 40% of patients, indicating that the majority of children benefited or were not affected by PICU care, regarding their HRQoL status. As clinically expected, nearly half of the cases with deterioration were trauma patients. Overall, 38% of the cases showed an improvement in HRQoL. As also expected, a higher improvement was seen in the elective admission patients, in non-trauma cases, and in patients with no need of mechanical ventilation.

Vector analysis also adds information from the perspective of morbidity among this population, showing that higher numbers of vector/case mean more heterogeneity and morbidity in the sample; in this study, after excluding perfect health states, we found more heterogeneity in the sample at follow-up (0.65 vs. 0.59 vector/case at preadmission).

These results clearly demonstrate that studies about HRQoL should incorporate measures of baseline status and should be focused on changes in the patient level rather than on the analysis of mean values for groups of patients. Despite the importance of individual measures, we do not endorse any use of these HRQoL values to guide clinical decisions in individual patients; individual results should only be used to evaluate and improve health care delivery.

The present study has several limitations. The problems of using proxies to evaluate HRQoL are well known, but there is also agreement that young and critically ill children are unable to understand or answer a questionnaire.[26-28] In these cases, using parents or guardians as proxies is better than using physicians/pediatricians.[26,28,29] Moreover, the need to have baseline data to compute changes in HRQoL favors the strategy of interviewing proxies to evaluate preadmission status as close as possible to PICU admission, with the purpose of preventing and reducing recollection bias.

The 6-month time we defined to follow-up may be debatable, because during this period children may have suffered events not related to PICU admission that could alter their HRQoL or because this period may be insufficient to allow complete recovery of children more severely affected by the cause of PICU admission. Data were collected between 2002 and 2004, but we consider that this time lag did not interfere with the study results.

There are no studies assessing the validity and reliability of the HUI3 questionnaire specifically for the pediatric intensive care setting. However, HUI3 precursors were validated and used in the PICU population,[3,6,9,10,13] and the HUI3 itself has been extensively validated in different clinical conditions and in different countries.[15,20-24]

Other limitations of the study include the large number of children excluded due to age limitation of the HUI3 instrument and the exclusions due to study protocol, resulting in a small sample of the PICU population. In our study, initial and 6-month evaluations were done to 21 and 17% of the total population, respectively. These numbers are similar to values from an UK multicenter general PICU study (20%).[13] Other studies in the PICU setting range from 1% of total population in a study including only children with PICU length of stay higher than 28 days[9] to larger values in single PICU studies - 42,[6] 45,[12] 70,[9] and 77%.[10] If we consider only the eligible children (≥ 6 years), our values would be 62 and 49% for initial and follow-up samples, respectively, which are much closer to the values reported in single PICU studies. Larger and more representative samples need to be studied to confirm these findings and to allow identification of other variables that might predict improvement in children's health status before HRQoL-based decisions can be suggested for admission criteria and/or prognostic purposes.

As previously noted, there are few studies of HRQoL in the PICU setting, and this is the first study using the HUI3. Therefore, any comparisons should be very carefully analyzed, due to the differences in methodology and in the instruments used to assess HRQoL. Jayashree et al.[10] reported 35% improvement using the HUI2 categorical evaluation and Taylor et al.[11] reported 32% using the Glasgow Outcome Scale (GOS) in survivors to PICU care, values that are similar to our 38% improvement.

Using the HUI2 global score in a 1-year follow-up study of children admitted to a Dutch PICU, de Keizer et al.[7] reported 21% improvement, 26% deterioration and 52% of "no change" in HRQoL. The percentages of improvement and deterioration are close to each other, as in our study, but with very different absolute values. Differences in percentage of "no HRQoL change" might be due to the absence of trauma patients and a larger percentage of post-operative patients in their sample. Another possible explanation is the larger follow-up time, allowing the children who deteriorated at 6 months to improve and regain their previous preadmission HRQoL, as reported in other studies.[12,14]

Only 31% of our cases were in perfect health prior to PICU admission and 30% at follow-up, numbers that are similar to other studies. Using the HUI2 questionnaire, percentages of full health in PICU samples were reported as 32% at preadmission,[6] 27% at follow-up,[13] and 37% preadmission and 21% at follow-up.[10] Taylor et al.[11] reported, with the GOS, 29 and 15% of perfect health status at preadmission and follow-up, respectively, in an Australian PICU.

Mean HRQoL values of our sample are lower than those found in general populations[30] and in patients with other diseases that cause no or small lesions to the central nervous system[31,32]; are similar to those found in samples of children surviving brain tumors[25]; but are higher than those found in adults with stroke[30] and in blind children who were newborns with extremely low birth weight.[33] These low values might be due to the increasing number of children with chronic diseases that are admitted to the PICU, either in non-elective acute events or in elective admissions, and due to the higher impact of the developmental/neurological attributes on the HRQoL, in comparison to the physical attributes.

Despite HUI3 global score being similar at both evaluations, differences were found at individual level, with only a relatively small proportion of children having their HRQoL unchanged. Preadmission data are essential to evaluate changes at individual level and this is even more important in populations with high percentages of preadmission morbidity, like patients cared in the PICU.

Low preadmission HRQoL or severe disability should not be a reason, by itself, to exclude children from being cared in the PICU setting, as many of these children have benefited from pediatric intensive care.

Acknowledegments

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