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RESEARCH

Patient and Caregiver Perceptions of Health-Related Quality of Life in Children and Adolescents After Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract

Purpose The purpose of this study was to analyze the patients' and caregivers' perceptions of health-related quality of life (HRQOL) of pediatric allogeneic hematopoietic stem cell transplant (HSCT) recipients. The perceptions in HRQOL of patients and their caregivers were studied using PROMS (patient-reported outcome measures) questionnaires.
Methods Retrospective analysis of data from children and adolescents who underwent HSCT at our hospital between 2017 and 2022. The self-report and parent-proxy report versions of the Pediatric Quality of Life Inventory 4.0 generic core scales (PedsQL 4.0) were used to assess HRQOL in four areas (physical, emotional, social, and school functioning) as reported by patients aged ≥ 2 to < 18 years and their caregivers and evaluated 1 and 2 years after hospital discharge allogeneic HSCT.
Results We collected data on the HRQOL of 36 patients and their caregivers through self- and proxy-reports. More than 70% of children and their caregivers perceived good HRQOL in all areas both 1 and 2 years after allogeneic HSCT. Patients and caregivers largely agreed in their assessments, although caregivers gave slightly higher HRQOL ratings. Children aged < 10 years had higher HRQOL scores than adolescents at both time points. Patients with an HLA-mismatched donor were at greater risk of impaired HRQOL than those with an HLA-matched donor, particularly in terms of physical functioning.
Conclusions More than 70% of patients and caregivers perceived good overall HRQOL (total PedsQL score) 2 years after hospital discharge from the HSCT unit.

Keywords Hematopoietic stem cell transplantation · Quality of life · PedsQL 4.0 · Patient-reported outcome measures (PROMS)

Introduction

Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment for many diseases. Although the procedure is continuously evolving, it is a highly complex process that requires long hospital stays and frequent follow-up visits during the first year. Complications such as treatment-related toxicity, graft-versus-host disease (GVHD), and infections due to immunosuppression often result in even longer hospital stays [1].

The literature contains conflicting reports on the impact of HSCT on health-related quality of life (HRQOL), with some studies reporting that young HSCT recipients have worse HRQOL than their healthy peers [2–4, 7], and others find no significant differences [5]. In addition, parents of children who have undergone HSCT have rated their children's HRQOL lower than the children themselves [1]. While survivors of pediatric HSCT have been found to experience anxiety and depression, their emotional HRQOL does not appear to be significantly impaired [6]. Satisfaction with peer relationships positively influences HRQOL, especially among adolescents [8]. Factors associated with worse HRQOL after HSCT include late and chronic effects, fatigue, female sex, and GVHD [5]. No studies have analyzed patient or caregiver perceptions of HRQOL after HSCT in our country.

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Patient-reported outcome and experience measures are important tools for understanding aspects of HRQOL from the patient's perspective and identifying areas with room for improvement. The Pediatric Quality of Life Inventory 4.0 generic core scales module (PedsQL 4.0) is a validated tool included in the European Rare Disease Research Coordination and Support Action Patient Reported Outcome Measures (PROM) Repository. Among the specific modules, there is the PedsQL Stem Cell Transplant Module, but it has not been validated in Spanish, so it is discarded as the instrument of choice. This inventory (PedsQL 4.0)measures physical, emotional, social, and school functioning as reported by the patient (child self-report) and primary caregiver (parent-proxy report).

The aim of this study was to use the PedsQL 4.0 to assess patient and caregiver perceptions of HRQOL in children and adolescents after hospital discharge from the HSCT unit, with the ultimate aim of developing appropriate psychological interventions in areas with the greatest risk of HRQOL impairment.

Patients and Methods

Study Design

We conducted a retrospective observational study to explore patient and caregiver perceptions of the HRQOL of children and adolescents who underwent an allogeneic HSCT at the HSCT unit at Hospital Vall d'Hebron in Barcelona, Spain, between 2017 and 2019.

The study was approved by the ethics committee at Hospital Universitari Vall d'Hebron PR(AMI)24/2023.

Informed consent was obtained from each of the participants in this study.

Inclusion and Exclusion Criteria

Children and adolescents aged ≥ 2 to < 18 years who underwent HSCT during the study period and accept to participate were included. Pacients and caregivers were evaluated 1 year and 2 years after hospital discharge from the HSCT unit.

The pediatric patients included in the study with an indication for HSCT were diagnosed with malignant diseases such as leukemia, or non-malignant diseases, such as bone marrow failure syndromes, hemoglobinopathies, primary immunodeficiencies, or metabolic diseases.

Patients with language barriers, a diagnosis of intellectual disability and/or an autism spectrum disorder, and a second HSCT performed > 6 months after the first procedure were excluded.

The patient selection process is shown in Fig. 1.

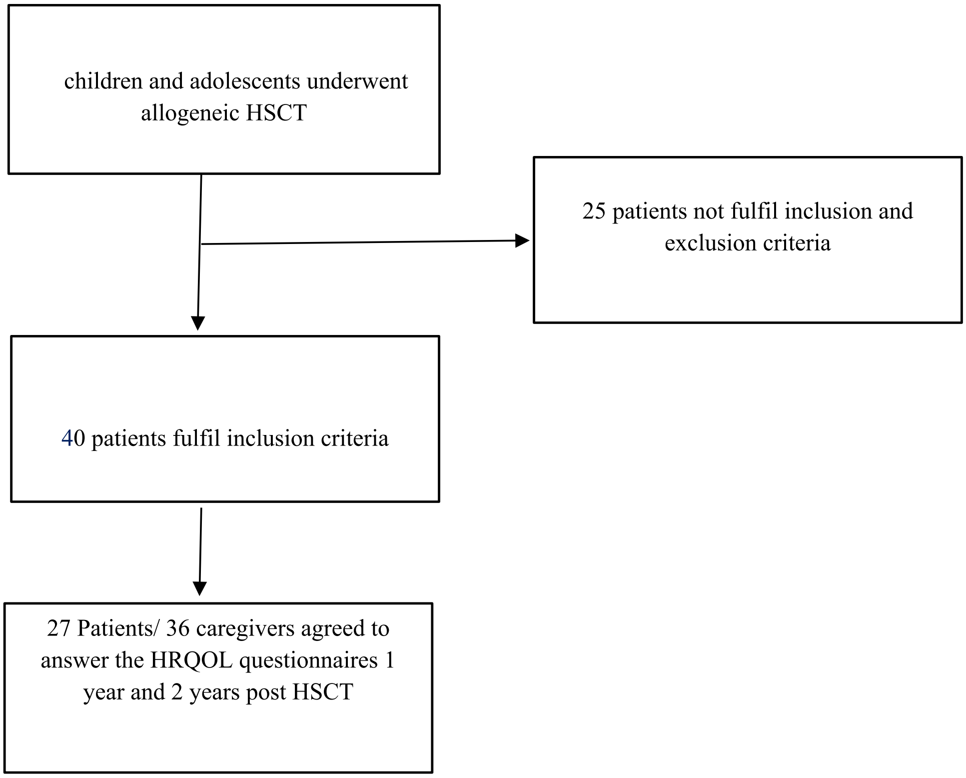

Fig. 1 Flowchart showing patient selection

HRQOL Questionnaires

Patient HRQOL was assessed using the child self-report [9, 10] and parent-proxy report [9] versions of the PedsQL 4.0, which provides a generic measure of HRQOL in four domains: physical, emotional, social, and school functioning. The self-report questionnaire consists of 23 Likert-type items, each with the same question: "In the past month, how much of a problem has this been for you…" For children aged 2–5 years only the caregiver version is available. Children aged 5–7 years are given four possible ranging from 0 ("never") to 4 ("almost always"). Older children (8–18 years) rate their answers on a scale of 5, ranging from 0 ("never") to 5 ("almost always").

The parent-proxy report version of the PedsQL 4.0 also has 23 items rated on a 5-point Likert scale (0 = never, 5 = almost always) [9].

Subscale scores for physical, emotional, social, and school functioning were computed as the sum of the items divided by the number of items answered. All scores were transfered to a 0–100 scale to enable comparisons between the age groups. Higher scores indicate better HRQOL.

The cutoff scores on the PedsQL 4.0 are 69.7 for the child self-report and 65.4 for the parent-proxy report. This score is obtained based on the standard deviation adapted to the pediatric population. As outlined in the aforementioned article, values below these cut-off points suggest that the children's quality of life may be impacted [9].

In this study, the PedsQL 4.0 was administered to patients and their primary caregivers at two time points: one year and two years after hospital discharge from the HSCT unit. While there are no strict universal recommendations regarding the optimal timing for assessing quality of life (QoL) after HSCT, both scientific literature and clinical practice agree on the importance of identifying the early impact, intermediate recovery, and potential chronic complications experienced by these patients. Patients and their caregivers completed the questionnaires during an in-person visit with the unit's psycho-oncologist at the hospital.

The effects of donor type (HLA-matched vs HLA-mismatched donors) and GVHD on perceived HRQOL were also assessed. GVHD in the study period was recorded dichotomously as "yes" or "no" and defined as acute GVHD grades II, III, and IV or chronic GVHD (moderate or severe). Acute GVHD was staged using the MAGIC criteria [11], while chronic GVHD was staged using the National Institute of Health consensus criteria [12]. These evaluations were made by the medical team.

Statistical Analysis

A descriptive analysis was made of all study variables. Categorical variables are expressed as absolute and relative frequencies and continuous variables as mean (SD) or median (interquartile range). The percentages of patients with HRQOL subscale and total scores above the cutoff were compared by age group and donor type.

The chi-square test and Fisher exact test were used as appropriate. HRQOL results for patients who experienced GVHD are described separately. Statistical analyses were made in Stata 15.1. A significance level of 0.05 was used for all analyses.

Results

We collected data on the HRQOL of 36 patients and their caregivers through self- and proxy-reports. Nine patients, under five years of age, only the perception of the caregiver could be obtained due to the developmental maturity of the patients and the characteristics of the PEDS.QL 4.0. Overall, 58.3% of the patients were aged 2–9 years, 61.1% had a non-malignant disease, and 69.4% had an HLA-matched donor (Table 1).

No associations were observed between HRQOL and sex or type of diagnosis (results not shown).

Patient and Caregiver Perceptions of HRQOL by Age Group and Time Since HSCT

Approximately 70% of patients in both age groups (< 10 years and ≥ 10 years) had good HRQOL (i.e., scores above the cutoff) in all the domains analyzed at 1- and 2-years post discharge HSCT unit. There was an increase in the percentage of adolescents with good HRQOL in the second year.

Table 1 Sociodemographic characteristics of patients

Patient characteristics	*n* = 36
Sex	
Female	13 (36.1%)
Male	23 (63.9%)
Age	
≥ 2 and 4	9 (25%)
≥ 5 and 9	12 (33.3%)
≥ 10 and < 18	15 (41.7%)
Diagnosis	
Malignant disease	14 (38.9%)
Non-malignant disease	22 (61.1%)
Donor type	
10/10 HLA-matched unrelated donor	13 (36.1%)
HLA-matched sibling donor	12 (33.3%)
HLA-mismatched donor	11 (30.6%)

Children Aged ≥ 5 and 9 Years

Children aged ≥ 5 and 9 years had higher rates of good HRQOL than adolescents both 1 and 2 years after hospital discharge from the HSCT unit.

On comparing the first and second years, there was an increase in the percentage of children with good HRQOL in the physical and social functioning domains and a slight decrease in that of children with good HRQOL in the emotional and school functioning domains. The total PedsQL 4.0 score also decreased slightly.

Adolescents

According to the total PedsQL 4.0 score, 46.7% of the patients in this age group were at risk of poor HRQOL at 1 year. Scores were particularly low in the emotional functioning domain in both periods, with 46.7% at risk after the first year and 38.9% after the second. Forty-percent of adolescents perceived poor physical HRQOL at 1-year post discharge HSCT unit, but this fell to 27.8% at 2 years.

Finally, social functioning scores indicated good HRQOL in 73.3% of adolescents.

Caregivers of Children Aged < 10 Years

In the younger age group, caregivers rated overall and physical HRQOL higher than the children, but their answers largely coincided.

Caregivers of Adolescents

The caregivers of the adolescents indicated that the emotional area had the lowest value (42.9%) 1-year post discharge HSCT unit, rising to 62.5% 2-year post discharge HSCT unit. These findings coincided with patient-reported, as they also scored lowest in the emotional area at both time points (53.3%/61.1%). Caregivers achieved higher total score of 57.1% and 75%, versus 53.3% and 72.2% for adolescents at both time points. It can be seen that both caregivers and adolescents increased their total score over the 2-year post discharge HSCT unit, indicating an improvement in their perception of HRQOL.

Caregivers scored higher on all subscales than adolescents, except for emotional functioning.

Details about patient and caregiver perceptions of HRQOL by age group and time since allogeneic HSCT are shown in Table 2.

Patient and Caregiver Perceptions of HRQOL by Donor Type and Time Since Allogeneic HSCT

Self- and proxy-reported scores were very similar when the results were compared by donor type.

Patients who had received a transplant from an HLA-matched donor had higher patient- and caregiver-rated HRQOL scores in all domains at 1 and 2 years after HSCT. The difference was particularly noticeable at 2 years.

Patients without an HLA-matched donor were at risk of poor physical and overall HRQOL at both time points.

Table 2 Comparison of patient and caregiver perceptions of health-related quality of life according to patient age 1 and 2 years after discharge HSCT unit. The first number in each cell refers to the number of patients or caregivers with a score above the cutoff in the given area (> 69.7 for patients and > 65.4 for caregivers). The second number corresponds to the total number of answers for this variable. The percentage refers to the percentage of answers above the cutoff. The *p* values were obtained by the chi-square or Fisher exact test, as appropriate

	Quality of life variables (PedsQL 4.0)	1-year post-discharge HSCT unit			2-years post-discharge HSCT unit		
		Age groups			Age groups		
		5–9 y	≥ 10 y		5–9 y	≥ 10 y	
		n > 69.7/*n* (%)	*n* > 69.7/*n* (%)	*p* value	*n* > 69.7/*n* (%)	*n* > 69.7/*n* (%)	*p* value
Patient	Physical functioning	9/11 (81.8%)	9/15 (60%)	0.0769	8/9 (88.9%)	13/18 (72.2%)	0.3122
	Emotional functioning	10/11 (90.9%)	8/15 (53.3%)	0.2455	8/9 (88.9%)	11/18 (61.1%)	0.0620
	Social functioning	8/10 (80.0%)	11/15 (73.3%)	0.2510	8/8 (100%)	14/18 (77.8%)	0.2844
	School functioning	7/8 (87.5%)	10/15 (66.7%)	0.3795	3/4 (75%)	13/16 (81.3%)	0.7385
	Total score (patient)	9/11 (**81.8%**)	8/15 (**53.3%**)	0.1132	7/9 (**77.8%**)	13/18 (**72.2%**)	0.1984
		≥ 2–9 y	≥ 10 y		≥ 2–9 y	≥ 10 y	
		n > 65.4/*n* (%)	*n* > 65.4/*n* (%)	*p* value	*n* > 65.4/*n* (%)	*n* > 65.4/*n* (%)	*p* value
Caregiver	Physical functioning	19/21 (90.5%)	9/14 (64.3%)	0.0088	16/18 (88.9%)	12/16 (75%)	0.8220
	Emotional functioning	19/21 (90.5%)	6/14 (42.9%)	0.0028	15/18 (83.3%)	10/16 (62.5%)	0.0709
	Social functioning	16/20 (80.0%)	9/14 (64.3%)	0.0236	14/17 (82.4%)	13/16 (81.3%)	0.1031
	School functioning	9/11 (81.8%)	6/14 (42.9%)	0.0356	9/12 (75%)	12/15 (80%)	0.0800
	Total score (caregiver)	18/21 (**85.7%**)	8/14 (**57.1%**)	0.0013	14/18 (**77.8%**)	12/16 (**75%**)	0.2476

In the sub-analysis of HRQOL by donor type, caregivers perceived slightly higher HRQOL than patients, but in both cases, physical functioning was the most affected area.

Details about patient and caregiver perceptions of HRQOL by donor type and time since allogeneic HSCT are shown in Table 3.

Impact of GVHD on Patient Perceptions of HRQOL

Of the 36 patients in the sample, four had GVHD at the time of the HRQOL assessments. They were all younger than 10 years old and had received a transplant from an HLA-matched donor; three of them had a non-malignant disease. Two patients had scores very close to the cutoff for overall poor HRQOL at 2 years.

The impact of GVHD on patient perceptions of HRQOL is detailed in Table 4.

Discussion

Allogeneic HSCT has improved survival rates in children with cancer and other life-threatening diseases in recent years. In this time, there has also been a growing interest in the study of long-term complications and the multidimensional effects of HSCT on HRQOL.

There is no consensus in the literature regarding the timing of HRQOL assessments [6]. However, the literature does point to the importance of systematically assessing HRQOL in order to develop specific interventions for patients who have undergone HSCT [1, 6, 7].

No differences in HRQOL were found by diagnosis, i.e., between cancer and other diseases. It is unclear whether such differences could be identified in future studies.

Table 3 Comparison of patient and caregiver perceptions of health-related quality of life according to type of donor 1 and 2 years after discharge HSCT unit. The first number in each cell refers to the number of patients or caregivers with a score above the cutoff in the given area (> 69.7 for patients and > 65.4 for caregivers). The second number corresponds to the total number of answers for this variable. The percentage refers to the percentage of answers above the cutoff. The *p* values were obtained by the chi-square or Fisher exact test, as appropriate

	Quality of life variables (PedsQL 4.0)	1-year post-discharge HSCT unit			2-years post-discharge HSCT unit		
		HLA-matched donor (related or unrelated)	HLA-mismatched donor		HLA-matched donor (related or unrelated)	HLA-mismatched donor	
		$n > 69.7/n$ (%)	$n > 69.7/n$ (%)	*p* value	$n > 69.7/n$ (%)	$n > 69.7/n$ (%)	*p* value
Patient	Physical functioning	15/19 (78.9%)	3/7 (42.9%)	0.0522	18/20 (90%)	3/7 (42.9%)	0.1396
	Emotional functioning	14/19 (73.7%)	4/7 (57.1%)	0.1582	15/20 (75%)	4/7 (57.1%)	0.2647
	Social functioning	15/18 (83.3%)	4/7 (57.1%)	0.1789	18/19 (94.7%)	4/7 (57.1%)	0.0402
	School functioning	14/17 (82.4%)	3/6 (50%)	0.3229	12/14 (85.7%)	4/6 (66.7%)	0.9668
	Total score (patient)	14/19 (**73.7%**)	3/7 (**42.9%**)	0.0685	17/20 (**85%**)	3/7 (**42.9%**)	0.0968
		$n > 65.4/n$ (%)	$n > 65.4/n$ (%)		$n > 65.4/n$ (%)	$n > 65.4/n$ (%)	*p* value
Caregiver	Physical functioning	18/24 (75%)	6/11 (54.5%)	0.2843	20/23 (87%)	5/11 (45.5%)	0.0243
	Emotional functioning	18/24 (75%)	7/11 (63.6%)	0.8229	18/23 (78.3%)	7/11 (63.6%)	0.1882
	Social functioning	19/23 (82.6%)	6/11 (54.5%)	0.1109	20/22 (90.9%)	6/11 (54.5%)	0.1117
	School functioning	11/18 (61.1%)	4/7 (57.1%)	> 0.999	13/17 (76.5%)	8/10 (80%)	0.1871
	Total score (caregiver)	18/24 (**75.0%**)	7/11 (**63.6%**)	0.4554	19/23 (**82.6%**)	5/11 (**45.5%**)	0.1092

Table 4 Quality of life scores in the physical, emotional, social, and school functioning domains of the PedsQL 4.0 for the four patients with graft-vs-host disease (GVHD) at the time of evaluation. Scores < 69.7 indicate a risk of poor HRQOL

	GVHD 1-year post-discharge HSCT unit					GVHD 2-year post-discharge HSCT unit				
	Physical	Emotional	Social	School	f. total	Physical	Emotional	Social	School	f. total
Patient 1	81	60	80	70	**74**	75	70	80	40	**67**
Patient 2	78	100	70	-	**82**	71	70	30	100	**68**
Patient 3	94	90	90	-	**92**	88	80	90	-	**86**
Patient 4	100	80	100	-	**94**	100	90	100	100	**98**

In our study, PedsQL 4.0 scores assessed 1 and 2 years after hospital discharge from the HSCT unit show that most of the children and adolescents analyzed had good HRQOL at both time points. Even higher rates were observed after 2 years, suggesting that HRQOL continues to improve with time.

Caregivers rated HRQOL slightly higher than the children and adolescents, but overall perceptions largely coincided, contrasting with previous studies where caregivers of pediatric HSCT recipients reported lower HRQOL scores than the children [1, 13]. The more favorable caregiver ratings observed in our study raise the question of whether perhaps parent and caregiver perceptions are influenced by a desire for "normality." Perceptions, however, can be influenced by a range of factors, including emotional distress, linked to the stress of the process and need for constant readjustments to the changing clinical situation, and children's desire to engage in similar activities to their peers.

Children aged < 10 years in our group had higher HRQOL scores than older children and adolescents both 1- and 2-year post discharge HSCT unit. This supports previous findings [6, 7] and suggests that transplantations performed at a younger age have a lower impact on HRQOL.

At both time points of the PEDS-QL 4.0 assessment, approximately half of the adolescents scored low in the area of emotional functioning, this finding expands upon earlier reports [14]. HSCT recipients are more likely to experience emotional distress and mental health issues than healthy peers, although this risk is not always reflected in emotional HRQOL scores [6]. Social functioning scores were higher in the younger age group. Twenty-five percent of adolescents perceived poor emotional and social HRQOL, but this rate increased to around 50% for patients with an HLA-mismatched donor. These findings are consistent with observations that satisfaction with peer relationships has a stronger influence on post-HSCT HRQOL in adolescents than in children [8].

Physical functioning was associated with the lowest patient- and caregiver-reported HRQOL scores in HLA-mismatched HSCT recipients. The results did not improve in the second year, supporting previous reports [5].

With regard to the impact of GVHD on patient well-being and their perception of HRQOL. These data only reflect the perception of four patients and therefore may not be representative of children and adolescents with acute GVHD.

As demonstrated in the results section, the emotional area is significantly impacted, particularly among the adolescents, and the physical area, notably among patients with HLA mismatch. These findings underscore the necessity to direct our attention and efforts towards these areas, with the aim of mitigating their impact on the patient's quality of life. Furthermore, recent talks at the EMBT 2025 Meeting in Florence by professionals in the field, including Hermioni, A., Sacaburri, E., highlighted the significance of adopting a multidisciplinary approach when working with these patients, emphasizing the need for a comprehensive, person-centered care approach.

We propose the creation of a group of adolescents guided by the psycho-oncologist and the physiotherapist of HSCT unit to be able to work on the physical and emotional spheres within the group context that breaks isolation and favors relationships with peers. The group will provide a safe space for adolescents to share their emotions and perceptions of their clinical situation, as well as to work on their physical functioning in a playful format. This will promote teamwork and mutual collaboration.

Our study has some limitations. First, our results should be interpreted with caution due to the small sample size. Second, although chronic illness has a significant influence on schooling, we were unable to assess school functioning in some cases, as not all patients were at school when the PedsQL 4.0 was administered. In addition, the COVID-19 lockdown led to interruptions in home or hospital-based schooling during the study period. Third, we were unable to compare changes in HRQOL before and after HSCT. We believe that future studies of HRQOL in transplant recipients should collect baseline information.

Conclusions

The health-related quality of life (HRQOL) of children and adolescents with chronic diseases is difficult to assess due to the subjective nature of the concept and the limitations of current measurement tools. Currently, the available scientific evidence on the impact of HSCT on HRQOL in children and adolescents is limited. No specific studies have been conducted in this area in our country, highlighting the need for further research.

The impact of HSCT on HRQOL varies from patient to patient and is influenced by medical factors, longer hospital stays, and psychosocial aspects. According to the perceptions of patients and caregivers who participated in this study, patients' quality of life improves over time. Two years after discharge from the HSCT unit, two-thirds of patients and caregivers report good levels of quality of life.

Patient-reported outcome measures should continue to be used as a means of rapidly identifying and implementing appropriate psychological interventions in children and adolescents with cancer and other chronic diseases. This will help to prevent any negative impact on their HRQOL and ensure they receive the best possible care.

Author Contributions All the authors contributed to the study concept and design. C.A prepared the approval documents to present to ethics committee at Hospital Vall de Hebron, M.B compiled the data, and A.V analyzed the data. M. B wrote the first draft of the article with

support and oversight from C.D-d-H and C.C. All the authors provided substantial contributions to subsequent versions of the manuscript and read and approved the final version.

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Data Availability No datasets were generated or analysed during the current study.

Code Availability All data and materials support the published claims and comply with feld standards.

Declarations

Ethical Approval The study was approved by the ethics committee at Vall d'Hebron Hospital PR(AMI)24/2023.

Consent to Participate The consent was obtained from each of the participants in this study.

Consent for Publication Not applicable.

Competing interest The authors declare no competing interests.

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