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ORIGINAL ARTICLE

Indication of neonatal palliative care: need for a guideline?

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Abstract

Objective: To describe the profile of newborns hospitalized in a neonatal intensive care unit of a tertiary university maternity unit from August 01, 2016 to March 31, 2018 and to evaluate how many would be included in palliative care, analyzing the implanted therapy. **Methods:** A retrospective study was performed, analyzing patients' charts for data collection and descriptive statistical analysis. **Results:** In the study period, 262 medical records of patients admitted to the neonatal intensive care unit were studied. Of these, 196 had a good evolution, without complications and sequelae, without limiting pathologies, being excluded from the indication of palliative care. Forty-two died and 24 had diagnostic hypothesis of some life-limiting disease, but which evolved steadily and were discharged from the unit. For those who died even in the process of death, with a continuous infusion pump of resuscitation drugs, they underwent resuscitation maneuvers. None of the newborns studied was accompanied by the palliative care team because of the non-solicitation of neonatologists for the specialty. **Conclusions:** In this study, we observed a population with indication of palliative care that did not receive this care, due to lack of request of the team, either in the finitude group to qualify the death and grieving process, or those who were discharged from the unit with limitations of life. After analyzing these data, a guideline flowchart with criteria for eligibility for palliative care was done, aiming to assist in the decision and activation of the team.

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INTRODUCTION

Pediatric palliative care (PPC) is a new field of medical practice in our country, and it is necessary to address the various myths associated with this practice.

PPC is a holistic, interdisciplinary, family-centered health care program for children from birth to adolescence, with the primary objective of improving quality of life. PPC emphasizes communication, sharing, decision-making, psychosocial support, and management of various symptoms by helping to coordinate care for children with complex medical needs. A unique aspect of PPC is the emphasis on family-centered care.[1]

The American Academy of Pediatrics in its approach to palliative medicine supports an integrated approach that begins with diagnosis and continues throughout the course of the disease. Palliative care is appropriate from the neonatal age to late adolescence in individuals with a potentially life-limiting disease. This care is not limited to end-of-life and bereavement, and it can often be provided concurrently with curative therapy.[1]

Rapid technological progress in neonatology has enabled many newborns, who would die in the past, to survive. Thus, the probability of children surviving with severe disability increased proportionally, with a reduction in infant mortality, but with increased morbidity.[2,3,4]

When dealing with death in the pediatric age group, more than 50% of deaths occur in the neonatal period and in the first year of life. Many of these patients cannot be discharged and die in the hospital.

The need for pediatric palliative care in neonatal intensive care units (NICU) is significant. The American Academy of Pediatrics suggests early and integrated PPC for patients and the families of children facing life-threatening conditions.

Early and long-term introduction of such care can optimize family-centered care. This makes the approach possible to ensure that the treatment plan and goals align with those of the family. PPC involvement in neonatal end-of-life care remains underutilized.[4]

There are many risks and harms involved in the newborn long-term hospitalization, and a future life with permanent neurological damage may happen at times.[4]

As a result, resuscitation procedures and active treatment of very sick newborns with the potential risk of severe neurological sequelae have become a point of tension and controversy, which in many cases raises questions about complex maintenance decisions, withdrawal or non-introduction of new interventions.[4]

Mortality rates do not elucidate the way newborns die, or bedside actions. Consequently, discussions about what should be done are difficult to accomplish, because what is actually done is not really known.[4]

Despite the mortality reduction, death is still present in neonatal intensive care units. From this point on, the great ethical dilemmas begin regarding therapeutic measures with consequent life extension for children with reserved prognoses and limiting chronic diseases. This period ends up being more painful, as there is no change in the outcome, and interventions are no longer curative.[4]

The current scientific literature points to a list of serious diagnoses that should trigger the entry of Palliative Care in the Neonatal ICU for follow-up of patients and their families (Chart 1).[5]

From the bioethical point of view, failure to introduce or withdraw interventions in dying patients is usually recognized as morally equivalent, although this does not imply that both actions are equivalent from the legal point of view.[4]

The HMU (Municipal University Hospital) is a hospital located in São Bernardo do Campo, which is the reference public maternity hospital for the city, having 20 NICU beds.

In our service, we noticed difficulties in including and accepting palliative care in neonatal intensive care. Therefore, it is necessary to disclose the specialty, starting the process of continuing education with the health team involved in the care of these patients, as well as analysis of the main care failures. There is a lack of guiding protocols on the subject and well-defined eligibility criteria, because despite the importance given to the subject by international agencies and the growing worldwide concern, there are few descriptions in the literature.[6,7] In Brazil, there is a lack of information and studies aimed at newborns with life-limiting conditions, justifying the present research.

Chart 1. List of diagnoses that can trigger the follow-up of neonatal palliative care.

Diagnostics
• Trisomy of the 13
• Trisomy of the 18th
• Renal agenesis
• Bilateral renal polycystic disease
• Anencephaly
• Holoprosencephaly
• Severe anoxic injury
• Congenital hydrocephalus
• Myelomeningocele
• Fetal hydrops with anasarca
• Xipophagus Twins
• Tracheal agenesis
• Cystic adenomatous malformation
• Bullous epidermolysis

MATERIALS AND METHODS

We ran a retrospective descriptive study through the analysis of medical records of newborns admitted to the neonatal intensive care unit of the Municipal University Hospital of São Bernardo do Campo, from August 2016 to March 2018, aiming to describe the patients' profile, postnatal diagnoses, need for palliative care, checking how many had indications for palliative treatment, analyzing the evolution and the treatment implemented.

The deaths were categorized according to a model that took into account the dimensions of the physiological characteristics and the interventions received by the newborns.

The newborns were classified as stable or unstable. The instability classification meant that the newborns met two of the following criteria: persistent desaturation despite the offer of 100% FiO2 in invasive mechanical ventilation; hypotension despite volume infusion and vasoactive drugs; prolonged bradycardia or anuria for longer than 24 hours.

All infants who were not unstable according to these criteria were considered physiologically stable.

After this classification, the patients were placed in one of the following categories based on the intervention offered or withdrawal: 1) patients who died while receiving active cardiopulmonary resuscitation (CPR); 2) patients who died without active CPR, that is, without removal of interventions but CPR was not performed; 3) dying patients for whom death was inevitable and who died despite the introduction of new therapeutic investments such as vasoactive drug adjustment, exchange or introduction of antibiotics.

Not introducing interventions was defined as not introducing potentially life-prolonging treatments, which included not only not performing CPR but also not introducing any additional intensive interventions such as not changing ventilation despite hypoxemia, not providing additional vasoactive drugs despite hypotension, not introducing artificial nutrition. The withdrawal of interventions refers to the items listed.

The classification resulting from the affected organ (brain, kidneys, intestine, lungs, and heart) was also considered. Newborns who received continuous positive airway pressure (CPAP), biphasic positive airway pressure (BIPAP) and intermittent mandatory ventilation (IMV) were considered to have received ventilatory support for the purpose of this analysis.

All data necessary for the classification of neonatal deaths were collected from the electronic medical records and were randomly distributed for analysis by the investigators.

The following parameters were used to characterize the sample: date of birth, date of death, gestational age, fifth minute Apgar score, birth weight, cardiopulmonary resuscitation in the delivery room and during hospitalization, length of stay, differential diagnoses, presence of congenital anomalies, infection, intraperiventricular hemorrhages, heart disease, invasive mechanical ventilation time, use of dialysis and vasoactive drugs, home oxygen dependence, need for tracheostomy and gastrostomy

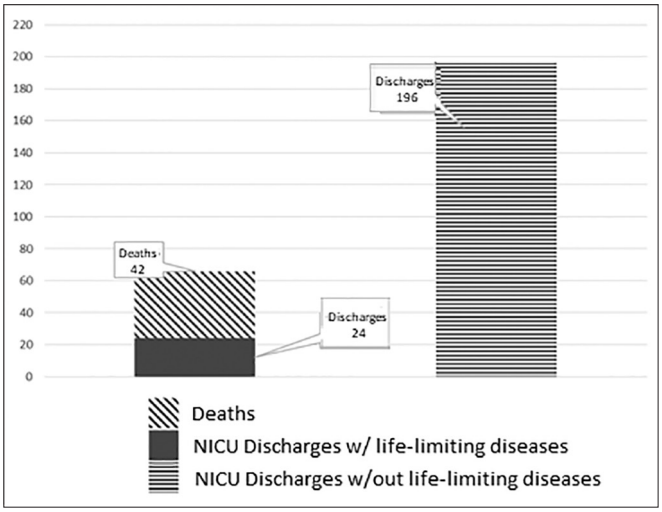
The statistical analysis was simply descriptive. The study began following the approval from the Research Ethics Committee of the department involved, the Research Ethics Committee of the institution (CAAE-9284241810000082 opinion - 2853294).

RESULTS

During the study period, there were 7,519 deliveries. A total of 262 patients with gestational age > 22 weeks who were admitted to the NICU and evaluated. Of this total, 42 patients died. 24 patients had life-limiting pathologies; however, they evolved well, with clinical stability, being discharged from the neonatal unit. (Graphic 1). The remaining 196 patients were discharged without sequelae. There were six deaths in the obstetric center.

In the group of 42 patients who died, extreme premature infants under 25 weeks prevailed, weighing between 501 and 750 grams. In this population, 54.8% had an Apgar score below seven in the fifth minute. During hospitalization, 57% of this population had sepsis, which was the leading cause of death. 23.8% had some type of intraventricular hemorrhage, of these, 70% of cases were classified as grade II, 20% grade III and 10% grade IV. Heart problems were identified by echocardiography in 45.2% of the cases; 9.5% underwent dialysis during hospitalization and 4.8% were diagnosed with non-evolving chronic encephalopathy (NECE). Two patients were born with diaphragmatic hernia, diagnosed prenatally and one with karyotype-confirmed Edwards Syndrome. (Table 1).

In this group, the average hospitalization duration was 8.8 days, with an average mechanical ventilation time of 8.2 days (Table 3). All patients used some type of vasoactive drug during hospitalization. For this study, we considered dobutamine, noradrenaline, adrenaline, dopamine, milrinone and E2 prostaglandin.



Graph 1. Outcome profile of NICU newborns.

Table 1. Characterization of the studied population that died.

		n = 42	%
GESTATIONAL AGE (weeks)	< 25	17	40,50%
	25 1/7 -28	14	33,30%
	28 1/7 - 30	4	9,50%
	30 1/7 - 32	2	4,80%
	32 1/7 - 34	1	2,40%
	34 1/7 - 36 6/7	1	2,40%
	≥ 37	3	7,10%
BIRTHWEIGHT (grams)	< 500	9	21,40%
	501 - 750	18	42,90%
	751 - 1000	5	11,90%
	1001 - 1500	3	7,10%
	1501 - 2000	1	2,40%
	2001 - 2500	0	0,00%
	> 2500	6	14,30%
APGAR INDEX (5^{th} minute of life)	< 7	23	54,80%
	≥ 7	19	45,20%
CARDIOPULMONARY RESSUSSITATION IN THE DELIVERY ROOM	ADRENALINE USE	5	11,90%
	OROTRACHEAL INTUBATION	42	100%
	CHEST COMPRESSIONS	5	11,90%
ASSOCIATED DISEASES	NNA*	23	54,80%
	SEPSE	24	57,10%
	IPVH**	10	23,80%
	HEART DISEASES	4	9,50%
	CARDIOPATIAS	19	45,20%
	DIALYSIS RENAL FAILURE	4	9,50%
	NECE***	2	4,80%

* NNA - neonatal anoxia
** IPVH - intraventricular hemorrhage
*** ECNE- non-evolving chronic encephalopathy

From this sample, all patients underwent cardiopulmonary resuscitation maneuvers upon cardiopulmonary arrest. In total, there were 86 episodes of cardiac arrest, with an average of two episodes per patient. In seven of the cases, even with continuous epinephrine use, patients underwent resuscitation maneuvers (16.6%).

The palliative care team was not called upon for follow-up in any of the cases.

The main diagnoses in the 24 survival cases with some pathology that would lead to life limitation were congenital heart disease, severe bronchopulmonary dysplasia, neonatal anoxia, two cases of myelomeningocele and one of Pierre Robin's syndrome.

There was a prevalence of newborns with gestational age greater than or equal to 37 weeks (33.3%) in this group, followed by 29.2% of newborns between 25 1/7 to 28 weeks. Regarding weight, the predominant range was newborns larger than 2500gr (33.3%). The Apgar score below seven in the fifth minute occurred in 33.3% of the newborns. During hospitalization, 62.5% of this population evolved with sepsis. 62.5% had some type of intraventricular hemorrhage, of which 66.7% of the cases were classified as grade I, 26.7% grade II and 6.6% grade III; in this group, there was no grade IV hemorrhage. Heart problems were found by echocardiography in 70.8% of cases; 20.8% underwent dialysis during hospitalization, and 16.7% were diagnosed with NECE (chronic non-evolving encephalopathy) (Table 2).

In this group, the length of stay in a neonatal intensive care unit was longer when compared to the group of deaths,

Table 2. Characterization of the population discharged from the NICU.

		n = 24	%
GESTATIONAL AGE (weeks)	< 25	3	12,50%
	25 1/7 -28	7	29,20%
	28 1/7 - 30	2	8,30%
	30 1/7 - 32	2	8,30%
	32 1/7 - 34	1	4,20%
	34 1/7 - 36 6/7	1	4,20%
	≥ 37	8	33,30%
BIRTHWEIGHT (grams)	< 500	0	0,00%
	501 - 750	5	20,80%
	751 - 1000	5	20,80%
	1001 - 1500	3	12,50%
	1501 - 2000	0	0,00%
	2001 - 2500	3	12,50%
	> 2500	8	33,30%
APGAR INDEX (5^{th} minute of life)	< 7	8	33,30%
	≥ 7	16	66,70%
CARDIOPULMONARY RESSUSSITATION IN THE DELIVERY ROOM	ADRENALINE USE	1	4,20%
	OROTRACHEAL INTUBATION	24	100%
	CHEST COMPRESSIONS	1	4,20%
ASSOCIATED DISEASES	NNA*	8	33,30%
	SEPSIS	15	62,50%
	IPVH**	15	62,50%
	HEART DISEASES	3	12,50%
	CARDIOPATIAS	17	70,80%
	DIALYSIS RENAL FAILURE	5	20,80%
	NECE***	4	16,70%

* NNA - neonatal anoxia
** IPVH - intraventricular hemorrhage
*** ECNE - non-evolving chronic encephalopathy

being 105 days, with an average invasive mechanical ventilation time correspondingly longer than 43 days (Table 3). The newborns remained more hemodynamically stable. Of the 24 patients, only 12 used vasoactive drugs at some time during NICU admission, including dobutamine, norepinephrine, adrenaline, dopamine, milrinone and prostaglandin E2. Of this population, only one child presented cardiopulmonary arrest and was successfully reversed after cardiopulmonary resuscitation maneuvers.

Table 3. Time of mechanical ventilation and stay in the NICU.

	DISCHARGES	DEATH
MEAN INVASIVE MECHANICAL VENTILATION TIME (days)	43	8,2
MEAN ICU STAY DURATION (days)	105	8,8

Considering both groups, we found in 38% (25/66) of patients some type of IPVH. In the group of children who were discharged from the unit, grade I predominated, which usually reabsorbs. In the group of deaths, grade II predominated.

Regarding the resuscitation attempts, 100% of the newborns who presented cardiopulmonary arrest received CPR, and in 16 cases, the death occurred after the first resuscitation, that is, the resuscitation failed (Table 4).

In cases of hospital discharge, only one patient required tracheostomy, two became oxygen-dependent and three required gastrostomy for food. All had significant delays in neuropsychomotor development and were stimulated daily by the physical therapy team during hospitalization.

There was also no request for the palliative care team to follow these patients, often there was no discussion for such care, even for those with severe limiting diseases and conditions present.

Table 4. Number of patients and resuscitation attempts.

Successful CPR	Number of patients
0	16
5	1
4	1
3	3
2	6
1	15

DISCUSSION

The situation analyzed in the present study corroborated the fact that there are a large number of extreme premature newborns maintained with invasive technologies, and often-ineffective therapies, as they had life-limiting pathologies without the possibility of control or improvement, and several of these newborns were near death. In some cases, treatment was utterly futile. These behaviors occurred due to ethical dilemmas and fears, generating therapeutic obstinacy in keeping alive "at any cost". In seven newborns, this situation was found with patients using continuous adrenaline, who evolved to death and who underwent the neonatal resuscitation protocol and, in this case, could be considered a death process and no longer cardiopulmonary arrest. This is a matter of concepts, one that is often overlooked, because an arrest means the abrupt and sudden interruption of circulation and breathing.[8,9]

The causes of death and complications presented in this study are similar to those found in Brazil. According to data from DATASUS, the main cause of death is associated with the neonatal period (74%), including sepsis,[10] diagnosis that predominated in the group of newborns in this study who died.

IPVH occurred in 38% of cases, a complication expected mainly in preterm infants below 1500g, which may lead to increased mortality and morbidity. Grade I IPVH predominated in the group of children who were discharged from the unit, and they were reabsorbed, in the group of deaths, grade II prevailed.

Regarding heart disease, 54.5% of the 66 patients had some type of cardiac pathology. Neurological changes also occurred in 47% of cases of NNA and 9% of NECE; 13.6% developed renal failure with dialysis.

The result was the presence of severely ill children with neuropsychomotor developmental delay sequelae, detected during hospitalization, some with oxygen-dependence and artificial breathing and eating pathways who did not receive special attention for symptom mitigation and quality of life gain. For those who died, we noticed that there was no quality of death of these children.

As observed in the results of this study, of the 262 patients, 66 (25%) had indication of palliative care, 42 patients died, and of the 24 who survived and were discharged from the intensive care unit, all had life-limiting disease. None of these patients received palliative care because there was no medical request for such.

The lack of medical request for assessment and follow-up of patients by the palliative care team may have occurred due to several factors such as resistance to accept the limiting situation, lack of information resulting from the current poor medical education on this subject, among others.[11,12]

Neonatologists and pediatricians bear the technical responsibility for appropriate medical care, bearing in mind the bioethical principles of beneficence and no maleficence, associated with the ethical responsibility of preserving the quality of life of their patients with complex clinical conditions, some with life-limiting conditions in a terminal stage.

Ethical clashes are part of this condition and, in these cases, a major clinical difficulty is to find therapeutic futility, keeping clear the boundary between what is scientifically adequate and ethical and what is considered useless diagnostic and therapeutic procedures, obstinate and disproportionate.[13] In this sense, the decision about what is a futile treatment and the indication of palliative care requires a broader discussion with the active participation of multidisciplinary teams and family members involved in child care.

Palliative care should be offered at the time of diagnosis and throughout the course of the disease with little expectation of cure, whatever its outcome. Palliative care aims to improve quality of life and meet the physical, psychological, social and spiritual needs of the sick child and his family, focusing on caring, advocating the prevention and alleviation of suffering to improve quality of life; and it may start with a combination of healing and prolonging the process of death, and afterwards in the process of mourning.[14,15]

Therefore, it is necessary that pediatricians have a palliative intention in the follow-up, depending on the case, with professionals specialized in palliative care. Even today, resistance to this type of care occurs among neonatologists. There is a syllabus deficiency among healthcare professionals, especially in medical education, to deal with limiting situations, especially those that correspond to the end of life.[16]

The training of human resources in palliative care should be carried out throughout the national territory, accompanied by a change in healthcare syllabus and implementation of the palliative care discipline in the training of these professionals, especially medical students, to bring change to healthcare paradigms, thus avoiding distortions in decision-making processes in the face of advanced and terminal diseases, as well as futile therapies.[17]

The goal of neonatal palliative care is to ensure quality-of-life improvement for patients and their families through fundamental measures, such as relief of physical symptoms and psychological, social, spiritual support for patients and families.[18] Currently, this topic has been discussed more frequently. Due to technological growth with new therapeutic possibilities, which was previously unviable, it has become feasible nowadays and it is possible to maintain the lives of extremely premature and/or severely ill premature children for long periods.[19,20,21,22] As a result, there is an increase in the number of children with various neurological and pulmonary sequelae.

The line of palliative care that has been previously much discussed in adults has now been discussed in neonatology and pediatrics, but there is still a long way to go mainly due to ethical challenges.

As in most retrospective studies, there were some limitations in the present study, related to the lack of information reported in the medical records and, therefore, the lack of evaluation and follow-up with parents, especially those whose children died in order to analyze the quality of the death process in the matter of following the family during the grieving process.

We concluded that the quality of death was poor due to the therapeutic investment without possibility of reversing the outcome. For those who survived, palliative follow-up could help structure a program with the intention of rehabilitating these patients. Bearing in mind that the most important thing is to bring life to days, quality, decrease of symptoms and not days to life, without worrying about the end-result. This can be costly and painful not only for the patient but also for their family members for not having an advanced care plan. The grieving process of family members is favored when they participate in the shared decision-making process of therapeutic limit, as it enables a greater experience of the disease.[23]

There is a great difficulty in literature descriptions of protocols with precise and clear indications of neonatal palliative care. Based on the collected data, we can see the limitation and the difficulty of the team in triggering and perceiving the candidates for this type of care. Therefore, we created an initial instrument and a guide, a flowchart of eligibility for neonatal palliative treatment, helping medical professionals on the need for evaluation and follow-up of these children by the palliative care team, identifying the end-of-life cases or not of newborns, directing therapeutic approaches to better care for these babies and their families (Figure 1).

Identify life-limiting condition
Life-limiting condition

- Kidney agenesis
- Inoperable heart anomalies or those of poor prognosis
- Structural organic anomalies
- Severe CNS (Central Nervous System) anomalies, anencephaly, hydrocephaly
- Metabolic conditions with low life expectancy despite treatment
- Skeletal dysplasia
- Hypoxic-ischemic encephalopathy
- Multiple-organ failure
- Grade IV intraventricular hemorrhage
- Diaphragmatic hernia
- Severe pulmonary hypoplasia
- Therapeutic impossibility < 22 weeks or < 500g)
- 13 and 18 trisomy and other genetic syndromes

Life-limiting conditions found?

NO → Follow treatment plan and design individualized for each patient

YES → Request assessment from the palliative care committee

Patient is terminally ill

NO → Carry out comfort measures to ameliorate symptoms that cause suffering, improving quality of life

YES → Talk to parents/guardians about prognosis and end-of-life → Assess treatment measures → Limit or interrupt treatment and/or procedures which extend the patient's life → Prepare family members for bereavement → humanize and provide better quality to the unavoidable death

This flowchart will be instituted at the Municipal University Hospital of São Bernardo do Campo in conjunction with a series of continuing educational actions for the involvement and understanding of the entire team, in order to promote reflection on the theme, in an attempt to integrate quality, ethics and humanization in healthcare.

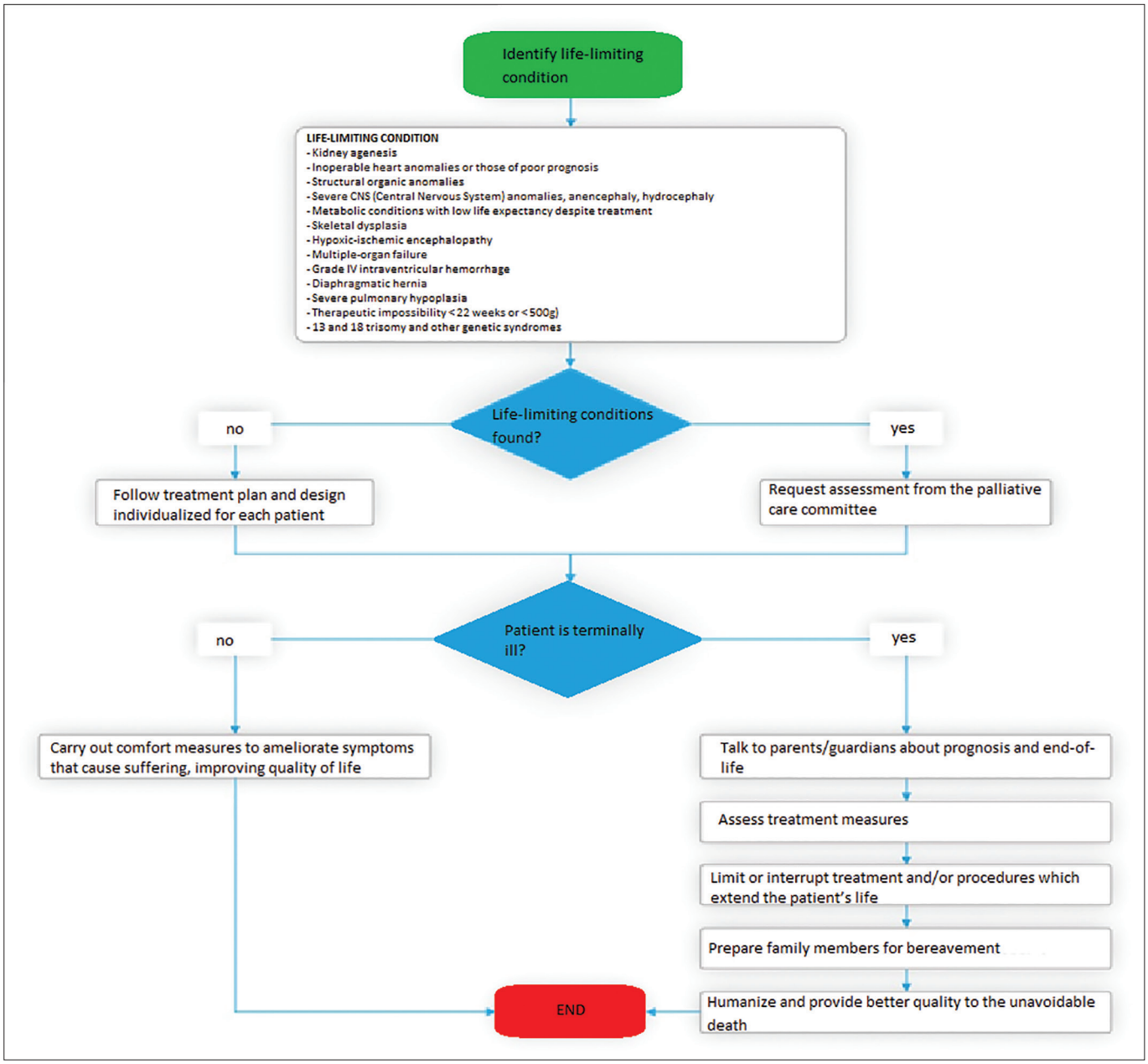


Figure 1. Flowchart of eligibility for neonatal palliative treatment.

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