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RESEARCH ARTICLE

Improving the quality of care in the molecular era for children and adolescents with medulloblastoma

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Abstract

Purpose Elevated mortality and morbidity rates persist in pediatric patients with medulloblastoma. We present a clinical audit of a real-world cohort of patients in search for pragmatic measures to improve their management and outcome.

Methods/patients All pediatric patients with medulloblastoma treated between 2003 and 2016 at a Spanish reference center were reviewed. In the absence of internationally accepted quality indicators (QIs) for pediatric CNS tumors, diagnostic, therapeutic, survival, and time QIs were defined and assessed.

Results Fifty-eight patients were included, 24% were younger children (< 3 years), 36% high risk (anaplastic, metastasis, or surgical residue > 1.5 cm^2), and 40% standard risk. Five-year OS was 59.2% (95% CI 47–75); 5-year PFS 36.4% (95% CI 25–53). Five main areas of quality assurance were identified: diagnosis, global strategy, frontline treatment modalities, outcomes, and long-term and end-of-life care. A set of 34 QIs was developed and applied. Lack of central pathology review, delay in the incorporation of novel molecular markers, and absence of a neurocognitive and quality-of-life evaluation program were some of the audit findings.

Conclusions This real-world research study resulted in the development of a pragmatic set of QIs, aimed to improve clinical audits and quality of care given to children and adolescents with medulloblastoma. We hope that our findings will serve as a reference to further develop a quality assurance system with specific QIs for pediatric CNS tumors in the future and that this will ultimately improve the survival and quality of life of these patients.

Keywords Medulloblastoma · CNS tumors · Childhood · Quality assurance · Quality of care · Real-world studies

Introduction

Medulloblastoma is the most common malignant central nervous system (CNS) tumor of childhood, accounting for 20% of all primary CNS tumors among children [1, 2]. It is an aggressive, embryonal tumor that requires multimodal treatment to achieve the current survival rates (global 5-year

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OS of 56%; 67% for children > 4 years) [2, 3]. Performing gross-total resection (GTR) at the time of diagnosis and early delivery of age-adapted craniospinal irradiation (CSI) after surgery continue to be the leading prognostic factors. Hence, the importance of treating children with medulloblastoma in highly specialized centers and of developing quality assurance (QA) programs to ensure best patient care.

Another cornerstone is the knowledge gained on biological features of medulloblastoma over the last few years, which has led to the characterization of four molecular subgroups, with distinct histology, genetics, clinical behavior, and patient outcomes: sonic hedgehog (SHH), Wingless (WNT), group 3 and group 4 [4]. This new knowledge has been incorporated into the most recent 2016 World Health Organization (WHO) classification of CNS tumors [5].

In current clinical trials, histopathologic and molecular features are included in the treatment decision algorithms. This new molecular era will allow better tailoring treatment, optimizing survival and reducing long-term toxicities. Beyond that, new therapies are emerging, aiming inhibition of molecular targets involved in the pathogenesis of medulloblastoma, especially for the SHH-pathway tumors [6, 7]. However, there seems to be a significant delay in the incorporation of molecular advances into daily practice, particularly for patients treated outside clinical trials.

We present a study conducted at a Spanish reference center for pediatric oncology. The aims of this study were (1) to present a real-world cohort of children and adolescents with medulloblastoma treated at a large Spanish institution, (2) to search for weak points in their management that can be improved at a local/institutional level leading to developing a set of quality indicators (QIs), and (3) to analyze the application of molecular markers and their incorporation into clinical decision making.

Methods

Patient identification

The experience of one major Spanish pediatric cancer hospital (Hospital Niño Jesús-HNJ-, Madrid) was collected. The clinical database was queried for all patients with the diagnosis of "medulloblastoma" between 2003 and 2016. Local institutional approval was granted for the retrospective chart review as part of an educational project (Board Review Reference Number: R-0057/17).

Eligibility

Inclusion criteria were histologically confirmed diagnosis of CNS–medulloblastoma (according to the current version of the WHO classification at the time of diagnosis [5, 8, 9]), diagnosed between 2003 and 2016, age 0–21 years at diagnosis, and available clinical and follow-up data. Of note: patients diagnosed or receiving treatment elsewhere and referred to HNJ later on were eligible as well.

Record review

Data collected included baseline and diagnostic characteristics, primary tumor's characteristics, extent of disease, histology and molecular markers (beta-catenin, SHH, p53, *c-Myc, n-Myc*, and 6-monosomy), frontline treatment strategy and its deviations, toxicities, relapses and salvage treatments, if any, and outcome. Pathology records were reviewed in light of the latest 2016 WHO classification [5]; this nomenclature is used to present the results.

Size and location of primary tumor were assessed by the diagnostic magnetic resonance (MRI) scan. Standard Chang M-stage classification was used [10].

Extent of resection was determined from the operative report and post-operative MRI (within 48 h). GTR was defined as no evidence of enhancing tumor on post-operative imaging; subtotal resection (STR) as any surgical resection less than GTR, distinguishing residual tumors ≥ 1.5 cm^2; "biopsy only" was assigned to patients, whose operative note included that text.

In the absence of comprehensive molecular analysis for most patients, three risk groups were considered: younger children (age < 3 years), standard risk (SR), and high risk (HR). Patients > 3 years and with any of the following features were assigned to the HR group: postsurgical tumor residue ≥ 1.5 cm^2, anaplastic histologic subtype, or M+. Patients > 3 years and with none of these features were considered SR.

Chemotherapy (CT) modifications were defined as time-intensity deviations (delay > 1 week between cycles), dose-intensity deviations (> 10% dose reduction of CT agents), and/or CT agents withdrawal.

Toxicities were collected from the medical charts and evaluated following the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), v.4.03 [11].

Statistical analysis

The date of diagnosis was considered the date of the diagnostic MRI. Time to progression was calculated from the date of diagnosis to the date of radiologic progression. Survival was estimated using the Kaplan–Meier method; the exact log-rank test was used for comparisons of survival in different groups. Progression-free survival (PFS) was calculated as the time from diagnosis to the date of first progression or relapse, or the date of last follow-up. Overall survival (OS) was defined as the time from first diagnosis

to death of any cause or the date of last follow-up. The 95% confidence intervals (CI) were provided. The significance level was fixed for all p values under 0.05.

Analysis was performed using the free software R, version 3.4.0. The ability to do multivariate analysis was limited due to the small sample size and was, therefore, not performed.

Results

Patient demographics and presentation

Sixty-six patients were identified. Eight patients were excluded due to incomplete medical records (Fig. 1) yielding 58 eligible patients for the clinical audit. Baseline characteristics are shown in Table 1. Median age at diagnosis was 5.0 years (interquartile range, IQR 3.1–7.4). One patient was diagnosed of Gorlin syndrome after the diagnosis of medulloblastoma [12]. No other patient had relevant prior medical history or identified genetic disorders.

Biological features

Twenty-four patients were diagnosed with medulloblastoma after 2011 when the four molecular subgroups were defined [4]. The determination of molecular markers was not implemented locally until January 2013. From 2013, 19 patients were diagnosed, but only eight (42%) had an available complete molecular profile including Beta-catenin, p53, *c-Myc*, and *n-Myc*. All markers were negative in all eight cases. With the opening of the SIOP-PNET5 trial, central pathology review and molecular analyses have been implemented.

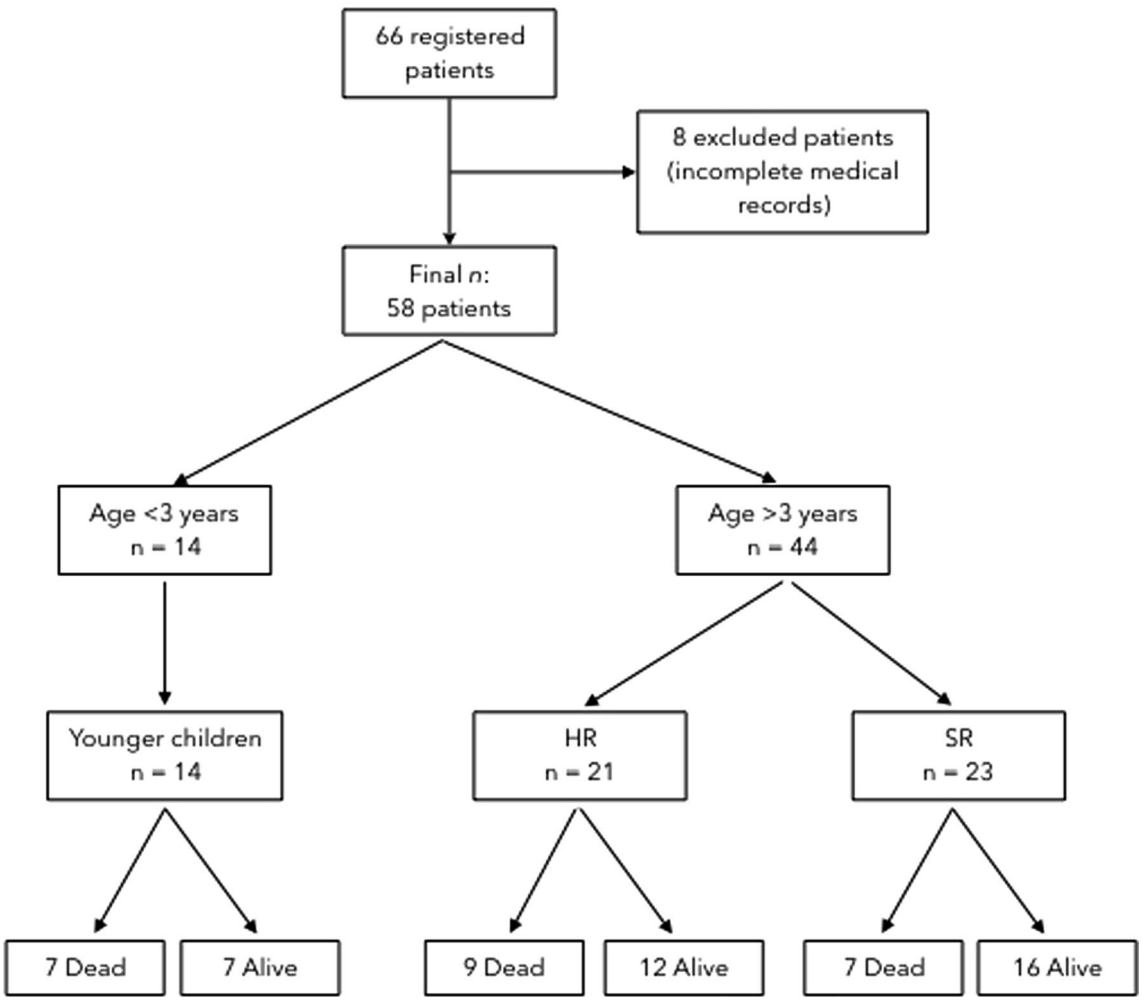

Fig. 1 Flow diagram of patients. *HR* high risk, *SR* standard risk

Table 1 Baseline and frontline treatment characteristics

	No.	%
Patient and tumor characteristics		
Sex ($n=58$)		
Male	40	69
Female	18	31
Age ($n=58$)		
< 3 years	14	24
> 3 years	44	76
Symptoms at diagnosis ($n=58$)		
Headache	32	55
Vomiting	41	71
Ataxia/gait impairment	24	41
Neurocognitive symptoms	10	17
Diplopia	8	14
Histology ($n=54$)		
Classic	42	78
Nodular/desmoplastic	5	9
With extensive nodularity	2	4
Large cell/anaplastic	3	5
Not otherwise specified (NOS)	2	4
M Chang stage ($n=56$)		
M0	37	66
M1	3	5
M2	4	7
M3	12	22
M4	0	NA
Type of metastasis (if M2/M3) ($n=16$)		
Nodules	3	19
Sugar coating	7	44
Both	5	31
Unknown	1	6
Frontline treatment		
Global strategy ($n=58$)		
SIOP-PNET4 [15]	27	47
SIOP-PNET5 (NCT02066220)	3	5
HART-Milan [16]	6	10
COG-ACNS0332 [17]	2	3.5
SFOP [13]	2	3.5
Head Start II [14]	11	19
Others[a]	7	12
Treatment modalities ($n=58$)		
Surgery	58	100
Gross-total resection	34	59
Subtotal resection	21	36
Biopsy only	3	5
Second look	4	7
GTR after second look	1	2
Radiotherapy upfront	41	71
> 4 years old	34	59
3–4 years old	7	12
Only local field (focal RT)	0	NA
Local field + CSI	41	71
Hyperfractionated RT	6	10
No RT upfront	17	29
Chemotherapy		
Systemic CT	57	98
Intrathecal CT	8	14
aHSCT	14	24
No CT upfront	1	2

aHSCT autologous hematopoietic stem cell transplantation, *CSI* craniospinal irradiation, *CT* chemotherapy, *GTR* gross-total resection, *NA* not applicable, *RT* radiotherapy

[a]The frontline treatment strategy changed over time throughout the years of the study, but was consistent for patients treated at Hospital Niño Jesús-HNJ—from the beginning. Younger children (< 3 years) were treated with radiation-sparing protocols: SFOP (French Society of Pediatric Oncology) [13] 2003–2005; Head Start II [14] 2005–2016. For children > 3 years, SR patients followed SIOP-PNET4 [15] 2003–2015, and SIOP-PNET5 (NCT02066220) since 2016; HR patients were treated following HART-Milan [16] until 2014, and COG-ACNS0332 (NCT00392327) since 2015. The seven patients that followed other frontline strategies were referred to HNJ at a later stage

First-line treatment

Global strategy

Frontline treatment strategy changed over time (Table 1). Younger children (< 3 years) were treated with radiation-sparing protocols: SFOP (French Society of Pediatric Oncology) [13] 2003–2005; Head Start II [14] 2005–2016. For children > 3 years, SR patients followed SIOP-PNET4 [15] 2003–2015, and SIOP-PNET5 (NCT02066220) since 2016; HR patients were treated following HART-Milan [16] until 2014, and COG-ACNS0332 [17] since 2015. Three patients were included in the SIOP-PNET5 trial; the rest of the patients were treated as "per protocol", as the respective trials were not opened locally at that time.

All treatment strategies included surgery with the widest possible resection. CSI was administered to all patients > 4 years and to most patients in the grey zone of 3–4 years. Patients < 3 years were treated following radiation-sparing protocols. Sixteen patients (27%) were treated with strategies designed to avoid radio-induced brain damage, whereas 41 patients (71%) were treated with radiation-inclusive regimens (one patient died shortly after surgery). Chemotherapy was used as consolidation in patients receiving radiotherapy (RT) upfront, and to delay RT in radiation-sparing protocols.

The audit findings for the main frontline treatment modalities (surgery, radiotherapy, chemotherapy, and autologous

hematopoietic stem cell transplantation), as well as for toxicity are shown in Supplementary Material 1.

Relapse and patterns of failure

Thirty-one (53%) patients experienced relapse or progression. Median time to first relapse/progression was 13.8 months (IQR 7.8–19.9). Twenty (65%) patients had received RT as frontline treatment. Thirteen patients ($n=58$, 22%) had a second relapse, five (9%) a third relapse, and three (5%) a fourth relapse. First relapse was local in 5/31 patients (16%), metastatic in 15 patients (48.5%), and combined in 11 patients (35.5%).

Outcomes and prognostic factors

Median follow-up for survivors was 5.2 years (IQR 3.1–9.0) (Fig. 2). For the whole population, 5-year PFS and OS were 37% (95% CI 25–53%) and 59% (95% CI 47–75%), respectively (Fig. 3a, b).

By risk group, 5-year PFS was 28% (95% CI 11–71%) for younger children (< 3 years), 25% (95% CI 11–57%) for HR patients, and 52% (95% CI 33–79%) for SR patients. Five-year OS was 44% (95% CI 23–84%), 51% (95% CI 32–81%), and 77% (95% CI 61–97%), respectively (Fig. 3c, d).

Metastatic disease at diagnosis and not having been irradiated on first line were variables significantly associated with worse outcome in the univariate analysis ($p<0.05$), with

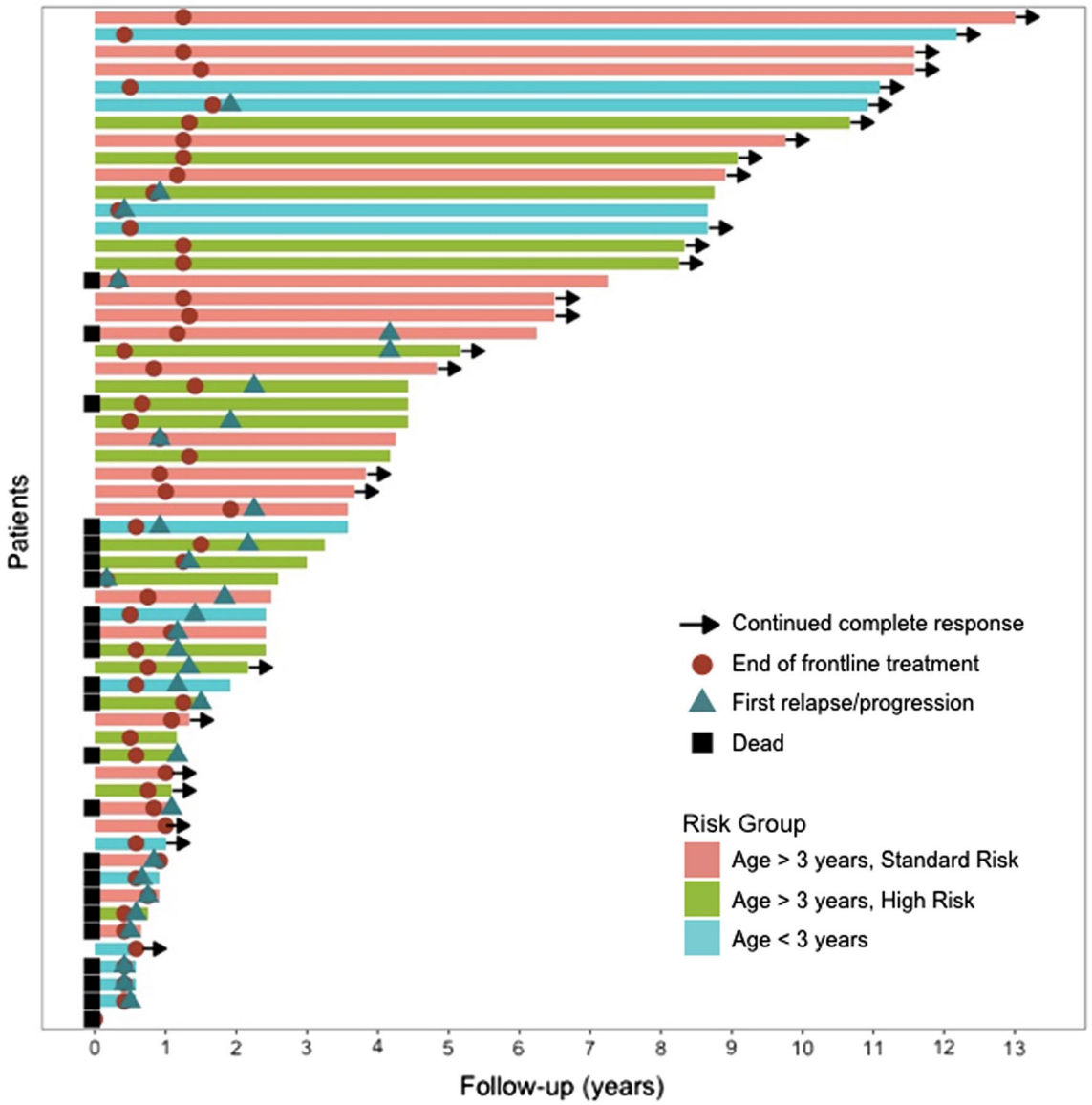

Fig. 2 Swimmer survival plot for all series

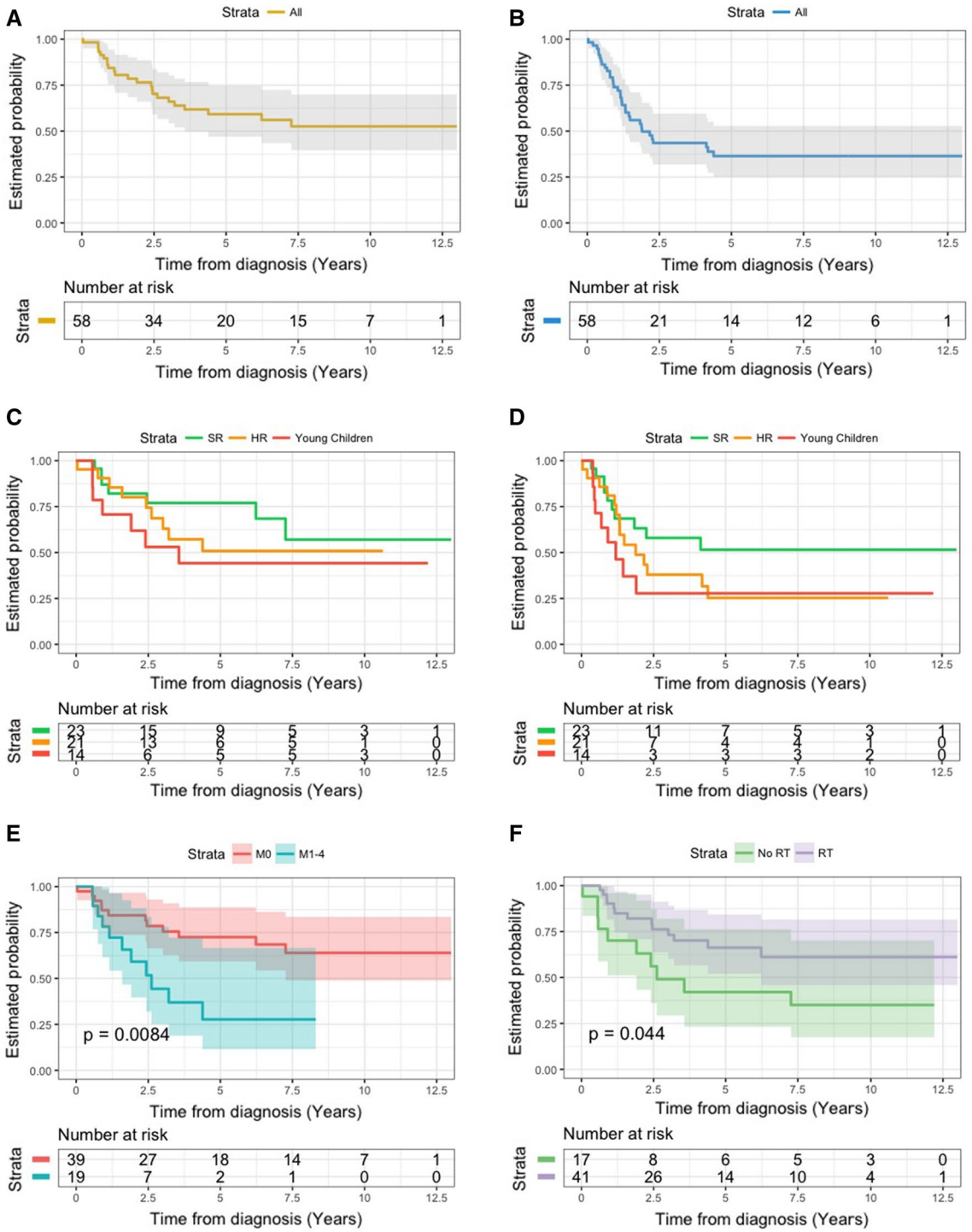

Fig. 3 Kaplan–Meier Curves: for all series (**a** overall survival. **b** progression-free survival); according to risk group (**c** overall survival, **d** progression-free survival); to disease extension at diagnosis (**e** overall survival); and to radiotherapy as frontline treatment (**f** overall survival). *HR* high risk, *RT* radiotherapy, *SR* standard risk

impact on both PFS and OS (Fig. 3e, f and Supplementary Material 2).

Improvement opportunities and quality indicators (QIs)

Upon review of the results of this audit, existing QIs in other areas of oncology, national, and consensus documents [18, 19], the study team devised a set of QIs that should be tested prospectively. Five main areas of QA were identified: diagnosis, global strategy, frontline treatment modalities, outcomes, and long term and end-of-life care. A set of 34 QIs addressing these areas was subsequently developed and applied to the results of the local audit.

The QA area "Diagnosis" included four QIs exploring how quickly patients are referred to specialized centers after suspicion or initial diagnosis, and the reliability of the pathology diagnosis. The QA area "Global strategy" included four QIs to analyze the inclusion of patients in clinical trials and the standardization of frontline treatments. The QA area "Frontline treatment modalities" consisted of 12 QIs evaluating the surgical outcomes, the experience of the surgical team and of the neuro-oncological team as a whole, the rapidness of access to radiotherapy and chemotherapy, and the treatment delivery in terms of compliance to the original treatment scheme. The QA area "Outcomes" encompassed nine QIs analyzing survival for the whole population and by risk groups, and acute toxicity. The QA area "Long-term and end-of-life care" included five QIs and explored long-term follow-up and sequelae and provided palliative care.

Table 2 includes the list of all QIs included, and the available results in our current data set which should serve for comparison in future studies.

Referral pathway

Another aspect of patient management analyzed in the clinical audit was the referral pathway, which is reflected in Fig. 4 and Supplementary Material 3. The initial diagnostic suspicion (with performance of CT or MRI) occurred at other institutions for 66% of the patients (38/58). The first line of treatment was administered at HNJ in 45/58 patients (78%); in four of them, initial surgery was performed in a different institution (but the rest of the first line was completed at HNJ). Three patients (5%) were referred to HNJ for aHSCT. The remaining 10 patients (17%) were referred to HNJ after relapse to receive salvage treatment.

Discussion

Our study constitutes the first step towards implementing a national QA system for children and adolescents with CNS tumors in Spain.

Despite overall improvements in the outcome of pediatric patients with medulloblastoma, mortality and morbidity rates are still unacceptably high, especially in patients with high-risk features [2]. On top of the general effort to develop new therapies [20], there is wide room for improvement to deliver high-quality care at a local/institutional level.

To improve the management of complex diseases such as medulloblastoma, it is crucial to identify the existing weak points. Clinical audits and QA programs constitute an essential part of clinical governance and good medical practice [18, 21–23]. Regular auditing practice allows to explore whether treatment strategies are being optimally delivered. There is an increasing international interest in the assessment of the quality of childhood cancer care using QIs [24]. In fact, some important steps have already been taken regarding the definition of the minimal standards of care for pediatric cancer patients. The best example is the SIOPe (European Society of Pediatric Oncology) guideline, a consensus document describing the minimum quality requirements for a pediatric oncology facility and providing a general directive [18].

In spite of this, and of the existence of several sets of QIs for adult cancer (e.g., for testicular cancer [25]), there is a lack of specific quality standards guidelines and QI systems for childhood cancer. A notable exception to this void is provided by a study of the Pediatric Oncology Group of Ontario (POGO), in which the authors developed a set of QIs for pediatric cancer care [26].

Moreover, the management of embryonal CNS tumors is particularly complex due to their aggressiveness and affected organ, the subsequent high severity of illness, the need for multidisciplinary and highly intricate treatments, and the potentially severe immediate and long-term toxicities derived from them. Thus, there is a need for specific QIs for the management of pediatric brain tumors, against which the overall performance of institutions and networks can be compared.

The set of proposed QIs is intended to provide a comprehensive, yet pragmatic tool to evaluate how children and adolescents with CNS tumors (specifically medulloblastoma) are being managed at a given institution. We believe these QIs to be straightforward and easy to collect for medium- or large-sized centers. They were chosen with the intention of being applicable to any kind of patients, particularly to those treated outside of clinical trials, and across all major pediatric oncology centers in Spain.

Table 2 Quality indicators and HNJ audit results

Areas of improvement	Quality indicators	HNJ audit
Diagnosis		
Quick referral after suspicion/diagnosis	Time to diagnostic MRI	4 weeks (IQR 2–7)
	Time to initial surgery	4 days (IQR 2–8)
Centralized diagnosis	% of centrally reviewed samples	14% (8/58)
	% of samples with basic set of molecular markers	14% (8/58)
Global strategy		
Inclusion in clinical trials	% of patients enrolled in clinical trials as frontline treatment	5% (3/58)
	% of patients enrolled in clinical trials as salvage treatment	6% (2/31)
Standardization of frontline treatments	Number of protocols/strategies followed within the same patient population	Homogeneous (1 strategy per risk group)
	Number of patients receiving treatments off-label	5% (3/58)
Frontline treatment modalities		
Surgical outcome	% of patients achieving GTR	59% (34/58)
	% of patients dying due to surgical complications	2% (1/58)
Experience of surgical team	Number of patients/year	3 new patients/year[a]
Rapid access to treatment	Time to RT ≤ 40 days (% of patients)	68% (21/31)
	Time to CT	42 days (IQR 39–47)
Treatment delivery	Frontline treatment duration	9.5 months (IQR 6–14.7)
	RT duration	43 days (IQR 42–48)
	CT duration	6.2 months (IQR 3.7–10.4)
	CT plan deviations	63% (34/54, 4 UNK)
	% of patients with CT dose-intensity modifications	26% (14/53, 5 UNK)
	% of patients with CT time-intensity modifications	42% (22/53, 5 UNK)
Experience of neuro-oncological team	Number of new patients/year	5 new patients/year[a]
Outcomes		
Survival	For the whole population	
	5-year OS	59% (95% CI 47–75%)
	5-year PFS	37% (95% CI 25–53%)
	By risk group	
	5-year OS—younger children	44% (95% CI 23–84%)
	5-year OS—high-risk	51% (95% CI 32–81%)
	5-year OS—standard risk	77% (95% CI 61–97%)
	5-year PFS—younger children	28% (95% CI 11–71%)
	5-year PFS—high-risk	25% (95% CI 11–57%)
	5-year PFS—standard risk	52% (95% CI 33–79%)
Toxicity	Frontline treatment-related mortality	4% (2/58)
Long-term and end-of-life care		
Long-term follow-up	% of survivors with grade 3–4 neurological disorders	81% (25/31, 4 UNK)
	% of survivors with grade 3–4 endocrine disorders	42% (13/31, 4 UNK)
Palliative care	% of relapsed patients receiving support from the local Palliative Care Unit	62% (15/24)[b]
	Time between engagement of the Palliative Care Team and death	Not collected
	% of patients deceased at home	Not collected

Median and interquartile range (IQR) are shown for time quality indicators

% percentage, *CI* confidence interval, *CT* chemotherapy, *GTR* gross-total resection, *HNJ* Hospital Niño Jesús, *MRI* magnetic resonance imaging, *OS* overall survival, *PFS* progression-free survival, *RT* radiotherapy, *UNK* unknown

[a]These numbers have been estimated considering the duration of the study (14 years) and (A) the number of included patients that received frontline surgery at HNJ ($n=41$) and (B) the number of registered patients ($n=66$). Both parameters may be underestimated

[b]From 2008, the hospital's Palliative Care Unit was created. Out of the 24 patients diagnosed and relapsed after its creation, 62% (15/24) were supported by the unit

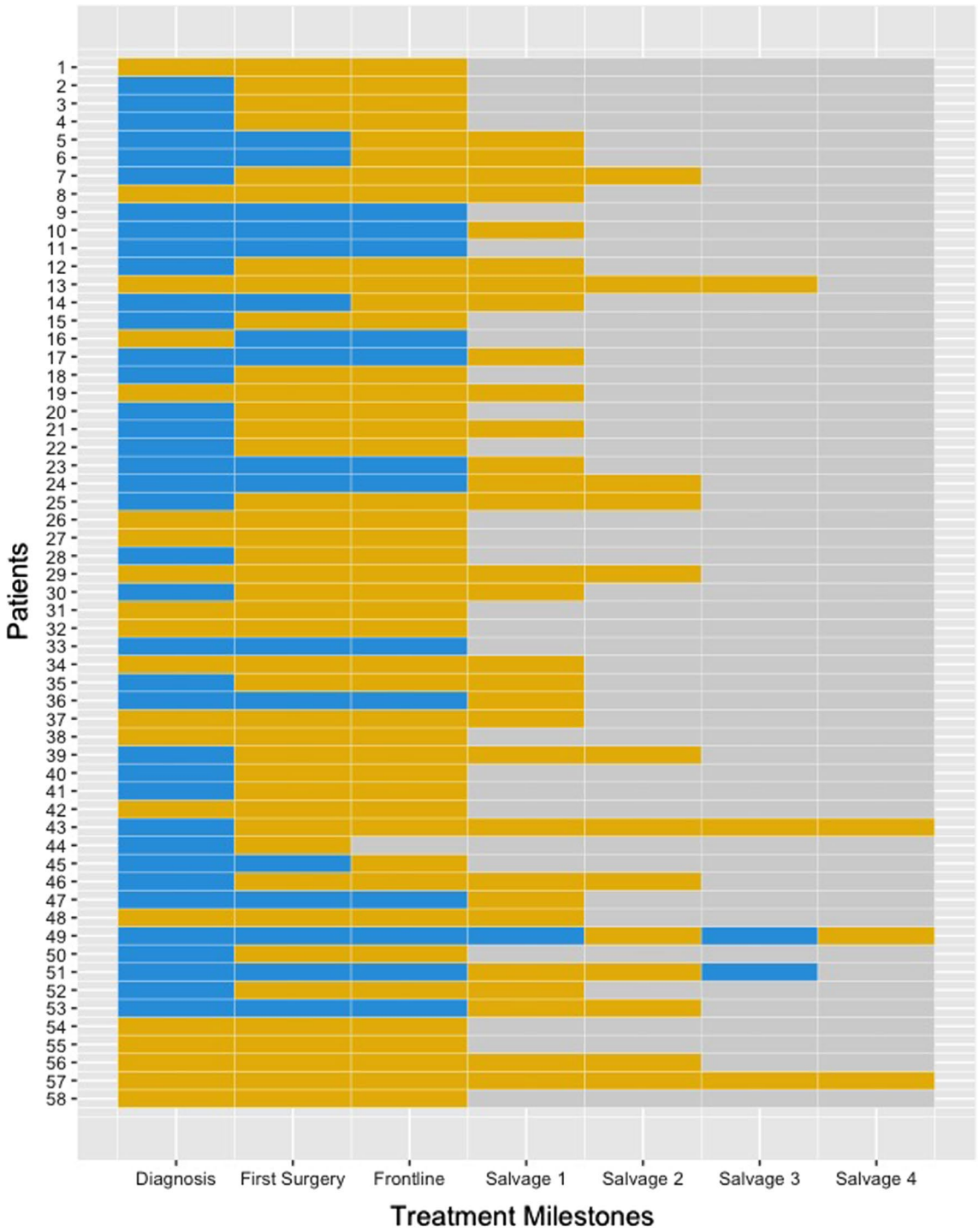

Fig. 4 Referral pathway. The colors reflect, where the treatment milestones occurred: Yellow, Hospital Niño Jesús (HNJ); blue, other institutions; grey, if not applicable (i.e., the patient did not undergo that milestone). Patients 9, 11 and 33 were referred to HNJ to undergo aHSCT. Note how most patients are diagnosed in other institutions and referred to HNJ for treatment. Note also how most salvage treatments are performed at HNJ, and how most patients, once referred to HNJ, stay there for the rest of treatment milestones

In fact, the wider aim of this study is to perform a national audit with the developed set of QIs, using the network of the CNS Tumors Group of the Spanish Society for Pediatric Hematology and Oncology (SEHOP), and in line with their recent national audit about the management of children and adolescents with CNS–PNET [27]. This will subsequently help develop quality clinical practice guidelines. Beyond

this, the set of QIs should be prospectively validated, ideally in the context of a wider international, collaborative study.

An important aspect to consider is how QA systems interact with clinical trials. Arguably, in this rare disease context, the enrollment of patients in frontline randomized clinical trials (RCTs) has become the standard treatment in pediatric oncology. However, international RCTs are not always accessible, for example, for particularly rare tumors or for time periods between the opening of consecutive trials. In addition, even though patient care in the context of RCTs is in general held to higher quality standards and close monitoring, the set of QIs produced in this work could be incorporated into the quality checks of trials as well. A common QA system would help ensure real benefit for patients treated in or outside RCTs, and hence help close the gap between trials and the real-world setting.

As for the concrete audit findings, our pragmatic approach to this real-world cohort of children with medulloblastoma has highlighted the strengths and weaknesses in their management at a local level, therefore, providing an example of how the developed set of QIs can be applied, and how this can help identify weak aspects that can lead to specific measures to improve patient care. The global outcome seems comparable to the results obtained in Spain and Europe. The 5-year OS of 59% is similar to the available European real-world registry data for CNS embryonal tumors, with a 5-year OS of 59.0%, and higher than the 5-year OS of 48% reported for Spain, although the patient populations might not be directly comparable as registry data would also include other high-risk embryonal tumors (previously called supratentorial PNET) [1, 28, 29].

In spite of the acceptable survival rates, several aspects could be improved at this institutional level: (1) the prevalent paper medical records added additional burden to auditing clinical practice; (2) no central pathology review was performed for most cases; (3) immunohistochemical molecular markers were not implemented until 2013 and genomic analyses are not widely available, with only 42% of the since then newly diagnosed patients having an available complete molecular profile; (4) in spite of over one-third (36%) of the patients not achieving GTR on initial surgery, only four of them (19%) underwent second-look surgery, as per decision of the multidisciplinary tumor board; (5) long-term toxicities, such as neurocognitive sequelae and hearing impairment, seem underreported [30–32]; and (6) none of the patients included in our study underwent quality-of-life assessments.

Some limitations of this study ought to be acknowledged. The retrospective nature of the study has magnified the problem of missing data, making some important information inaccessible. The monocentric nature of this work makes the resulting sample size ($n = 58$) inadequate for complex statistical analysis, and hence, the conclusions derived from survival analysis should be handled carefully.

However, the main aim of this study was to find aspects in the care of patients with medulloblastoma that could be improved at a local level; this monocentric approach to a referral institution serves its purpose in a very pragmatic way. The identified areas in need of improvement and the proposed set of QIs should undergo validation in prospective studies, but will be useful to compare subsequent audits conducted at our center over the following years. We hope that the QIs can be used within a national initiative and help building a common strategy to strengthen quality of care in our country beyond participation in international clinical trials.

A further strength of this study is being a real-world data cohort, which allows to draw conclusions that go beyond those driven from clinical-trial cohorts. Hopefully, this study will help to better understand the gap between clinical trials and real-world survival and to find ways to reduce this gap.

The main conclusion of this work is that there is wide room for improvement at an institutional level in the management of pediatric patients with medulloblastoma. Although the survival rates of this study are comparable to those achieved across Spain and Europe, there are several specific aspects that should be improved. The first step could be to implement a quality assurance system; this includes creating a database for systematic data collection and performing regular clinical audits. In lack of internationally validated quality indicators for the management of pediatric patients with CNS tumors, the QIs proposed in our study could be prospectively validated and used.

Beyond the local level, there is a strong need for collaboration in the treatment of complex CNS tumors such as medulloblastoma. Single institutions, especially reference centers, will benefit from an enhanced national network and from the implementation of well-structured referral pathways; and vice versa, the national (and European) network would benefit from using a network of institutions with good practices, high-quality data, and regular clinical auditing.

We conducted a pragmatic study, in search of areas of improvement in the management of pediatric patients with medulloblastoma. We hope that our findings will serve as a reference to further develop a quality assurance system with specific QIs for pediatric CNS tumors in the future and that this will ultimately improve the survival and quality of life of these patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments and comparable ethical standards.

Informed consent Due to the retrospective nature of the study, formal consent was not required.

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