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Retrospective Cohort Study

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Malignant transformation and tumour recurrence in sacrococcygeal teratoma: a global, retrospective cohort study

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Introduction: Sacrococcygeal teratoma (SCT) is a rare congenital tumour. The risk of malignancy and recurrence is not well defined. Previous studies are small and report differing conclusions about the timing of surgery and the duration of follow-up. The authors studied the risk of malignant transformation and SCT recurrence after surgery to address these gaps.

Methods: This was a global retrospective cohort study. Data of consecutive SCT patients was obtained from 145 institutes in 62 countries. Malignant transformation, defined as malignancy at initial resection, malignant recurrence or death due to malignancy, and its risk factors were analysed.

Results: Of the 3612 included patients, 3407 entered analysis. The risk of malignant transformation of the initial tumour was 3.3, 5.1, 10.1, and 32.9% at age 3 months, 6 months, 1 year, and 2 years, respectively. After 6 years, the censored risk of malignancy (64%) did not further increase. Recurrent SCT was diagnosed in 349 (10.2%) children with 126 (36.1%) malignant recurrences. Risk factors for recurrence were Altman type II [odds ratio (OR): 1.6, 95% confidence interval (CI): 1.2–2.2], Altman type III (OR: 1.6, 95% CI: 1.2–2.3), initial immature histology (OR: 1.9, 95% CI: 1.4–2.6), and initial malignant histology (OR: 4.0, 95% CI: 2.9–5.4).

Conclusion: The risk of malignancy at initial resection in SCT increases with age reaching a plateau at 6 years of age. Recurrence after resection occurred in 10% of patients and 36% of these were malignant at that time. Altman type II or type III, and immature or malignant histology were associated with recurrence.

Level of evidence: Level III.

Keywords: malignant transformation, recurrence, sacrococcygeal teratoma

Introduction

Sacrococcygeal teratoma (SCT) is the most common neonatal tumour with a reported incidence of one per 14 000–35 000 live births[1]. The preferred treatment for SCT is complete resection at a young age. However, there is no generally accepted age at which resection should be done. Some clinicians advocate early surgery to minimise the risk of malignant tumour transformation as malignancy rates up to 70% have been reported if SCT is resected at age one year or older[2]. Others claim that surgery at a young age may lead to more operative and postoperative complications[3].

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Tumour recurrence after surgery occurs in two to 33% of patients and decreases the overall 10-year survival ranging from 60 to 92%[2,4,5]. Recurrent SCT is much more often malignant than SCT at initial resection with yolk sac tumour (YST) found in 22–56% of recurrences[1,6–8]. Definitive risk factors for tumour recurrence are relatively unknown, although tumour histology and completeness of resection, including coccygectomy, are reported as potential risk factors for recurrence[2,5]. However, most studied series are relatively small due to the rarity of the disease and the results are often contradictory. Furthermore, the duration of follow-up varies in the existing literature, which likely impacts the reported recurrence rate; although most recurrences present within 3 years after initial SCT resection, late recurrences up to 15 years have been described[1,5]. From a clinical perspec tive, there is no consensus regarding the appropriate duration of oncological follow-up of SCT patients.

The vast majority of the reported series of patients with SCT are from high-income countries (HICs) in which SCT patients are operated on within a few weeks after birth. The number of publications about SCT from low-income countries (LICs) and lower-middle-income countries (LMICs) is very limited[9,10]. Recently, unacceptable differences in mortality for congenital gastrointestinal anomalies have been shown in LICs, compared to upper middle-income countries (UMICs), and high-income countries (HIC's)[11]. It is unknown if these differences are also present for SCT.

Given these uncertainties, we aimed to estimate the risk of malignant transformation of untreated SCT at different ages and, hence, the optimal time for resection. Furthermore, we aimed to identify factors associated with recurrent SCT and finally compare the treatment and outcome of SCT patients from different income countries.

HIGHLIGHTS

- This global retrospective cohort study includes 3612 sacrococcygeal teratoma patients from 62 countries worldwide.
- The risk of malignant transformation increases with age.
- The risk of recurrent sacrococcygeal teratoma after initial resection is 10%.
- If possible, complete resection of sacrococcygeal teratoma is recommended before age 1 month.
- Postoperatively, 6 years of follow-up is advised to detect possible recurrence.

Methods

Study design and participants

We did a global retrospective cohort study of SCT patients: 'The SCT-study' STROBE (The Strengthening the Reporting of Observational Studies in Epidemiology) and strengthening the reporting of cohort, cross-sectional, and case–control studies in surgery (STROCSS) (Supplemental Digital Content 1, http://links.lww.com/JS9/D406) 2021 guidelines were followed[12,13].

We recruited as many patients from participating hospitals as possible regardless of geography. Paediatric surgeons and paediatric oncologists were invited to participate in the study through personal communication, the European Paediatric Surgeons' Association (EUPSA) Network Office, PubMed publications, and a network of national and international study leads. Study information was provided in English, Spanish, French, and Russian. Participation was voluntary; no payment was made for data collection. Centres, which could include ten or more patients were invited to participate. An exception was made for centres from LICs and LMICs. For these centres, the minimum number of inclusions was set at five. The Supplementary Appendix (Supplemental Digital Content 2, http://links.lww.com/JS9/D407) provides an overview of the participating countries.

Due to the rarity of the condition, no sample size calculation was done and all eligible patients were included. Consecutive patients treated for SCT between 1982 and 2020 or a shorter time period in this era could be included into the study. Exclusion criteria were (a) born before 1982, (b) born after 2020, or (c) SCT as part of Currarino Syndrome (CS) as the risk of malignant transformation in (CS) may be reduced compared to 'ordinary' SCT[14,15]. The exact period of time for inclusions was determined by each individual participating centre as long as all consecutive patients in the chosen period were included.

All participating centres obtained local approval to participate in the study following their own legal and ethical regulations. Data transfer agreements were used to guarantee safe data use and storage.

Charts were reviewed by the individual local investigator. Data were validated with warning messages about possible errors when entered in Castor Electronic Data Capture (EDC). Furthermore, Castor files were structured so that out-of-range values could not be entered. Dependency fields were used for data and included initial resection, recurrence, death and follow-up. Furthermore, overall data distribution and frequencies in SPSS were checked to detect invalid entered data.

Procedures

Data was anonymized by the local investigator to transform individual patient data into general anonymous information. Transformed patient data were uploaded with a personal link in Castor EDC and encrypted[16]. Every participating centre had only access to its own transformed patient data.

Included data was carefully selected by a group of experienced paediatric surgeons with interest in SCT treatment and was chosen based on main outcome variables used in previously published studies.

Collected data included generic and condition-specific variables. Generic variables included: country, sex (male/female/unknown), age at diagnosis (days), preoperative imaging modalities (none/ultrasound/computed tomography/MRI/unknown), initial tumour resection at the participating centre (yes/no/unknown), age at initial resection (days), outcome (survival/deceased/unknown), age at follow-up (days), age at death (days), and cause of death. Condition-specific variables were Altman classification (I/II/III/IV/unknown)[17], CS (yes/no/unknown), initial SCT treatment (che motherapy/surgery/no treatment/unknown), pathology (mature/immature/malignant/unknown), recurrence (yes/no/unknown), per iod between birth and recurrence (days), detection of recurrence (clinical examination/imaging/AFP/unknown), serum AFP-level at recurrence (μg/l), recurrent SCT pathology (mature/immature/malignant/unknown), and treatment of recurrent SCT (chemother apy/surgery/no treatment/unknown).

Cause of death was collected as a free-text category. Participating country was used to categorise the country's income status into LICs, LMICs, UMIC, and HICs according to the World Bank criteria[18].

Statistical analysis

Data are presented as mean with standard deviation (SD) if normally distributed and median with interquartile range (IQRs) if skewed; count data are presented as numbers and percentages. To assess malignant transformation of initial SCT and risk of recurrence over time, Kaplan-Meier curves were used.

Identification of factors associated with recurrent SCT was done by univariable and multivariable logistic regression analysis. All variables included in multivariable logistic regression analysis had maximum of 6.8% missing data. Sensitivity analysis was performed to analyse the effect of data imputation on the results of the multivariable logistic regression analysis.

Forward Wald selection was used to select variables significantly related to recurrent SCT. We report variables with the odds ratio (OR) and accompanying 95% confidence interval (CI).

Differences in patient demographics between country income were analysed with Fisher exact test for categorical variables, one-way ANOVA for normally distributed continuous variables, and Kruskal–Wallis test for non-normal continuous variables.

Statistical analyses were performed using SPSS for Windows version 25.0 software (SPSS) and Graph Pad Prism 8 (Graph Pad Software, Inc.). $P < 0.05$ was considered statistically significant.

Definitions

SCTs were classified according to the criteria proposed by the Surgical Section of the American Academy of Paediatrics[17]. Recurrence was defined as relapse of SCT at least 3 months after initial resection[15]. Recurrent SCT before 3 months is unlikely and is probably due to incomplete resection, therefore, these recurrences were excluded from data analysis. Malignancy-free survival was defined as time from birth to malignancy or death due to malignancy. Patients were censored at the number of days from birth to resection. In case of malignant recurrence or death due to malignancy, the number of days from birth to recurrence detection or death was used.

Variables investigated for recurrent SCT, with their respective categories, were Altman classification (I, II, III, and IV), histology (mature, immature, and malignant), age at diagnosis (days), income of the country (LIC, LMIC, UMIC, and HIC), and age at initial resection (days).

Results

Patient characteristics

In total, 145 centres from 62 countries treated 3612 patients for SCT. In 205 patients, SCT was associated with CS. These patients were excluded from the analysis. In total, 3407 patients were included in the study. Patient characteristics for the total population are described in Table 1.

Preoperative imaging was done with ultrasound in 595 (17.5%), CT in 280 (8.2%), and MRI in 526 (15.4%) patients, respectively. A combination of imaging modalities was performed in 1400 (41.1%) patients. In 606 children (17.8%), no imaging was performed or was unknown.

Surgery was the initial treatment in 2947 (86.5%) children. Surgery and chemotherapy were applied in 388 (11.4%) patients. Sixteen (0.4%) children received only chemotherapy. Furthermore, 13 (0.4%) children received no treatment and died immediately after birth due to bleeding or respiratory distress. In 43 (1.3%) children, treatment was unknown.

Overall for the entire cohort, the median follow-up was 5.1 years (IQR 2.3–9.2 years) after resection. In total, 140 (4.1%) patients died at a median age of 10.2 months (IQR 3 days–3.2 years). Ten years after the initial resection, 505 patients remained in follow-up. The 5-year survival was 95.4% and 10-year survival was 94.8%.

Malignant transformation

Histological diagnosis after initial resection was mature teratoma in 2168 patients (63.7%), immature teratoma in 625 (18.3%), and malignant teratoma in 366 (10.7%). In 248 patients (7.3%), the histological diagnosis was unknown. The proportion of patients with malignant SCT increased with age. The probability of malignant transformation diagnosed at initial resection starts to increase directly after birth and increases further with age. The risk was 3.3, 5.1, 10.3, and 32.9% at 3 months, 6 months, 1 year, and 2 years, respectively (Fig. 1). After 6 years of age, the probability of initial malignant SCT did not further increase (64.2%). After 6 years, only one patient presented with an initial malignant SCT at the age of 8 years.

Malignancy-free survival including initial malignancies, malignant recurrences and deaths due to malignant disease, was 94.7% at age 1 year and 88.2% at 2 years (Fig. 2). Probability of overall malignancy-free survival remained relatively stable after the age of 6 years at 80.2%. After this period, four late malignancies were found; one initial malignancy, one malignant recurrence and two deaths due to malignancy. Late malignancies up to 15 years of age were found with an overall malignancy-free survival of 79.1%.

Recurrent sacrococcygeal teratoma

Three hundred forty-nine children (10.2%) developed recurrences at a median period of 11.4 months (IQR 6.4 months–1.8 years) after surgery. Ninety-six per cent of recurrences presented within the first 5 years after initial resection with a probability of recurrence-free survival after 5 years of 85.9% (Fig. 3). Late recurrences occurred up to 22.1 years after initial resection. Forty children died after recurrence at a median age of 15.6 months (IQR 6.2 months–2.3 years) after recurrence detection. Thirty died due to tumour progression or complications of chemotherapy. In 10 patients the cause of death was unknown. The other 284 survived; in 25 patients the outcome after recurrence was unknown.

Recurrent SCT was resected in 131 children, in 157 resections was combined with chemotherapy, and 33 children were treated with chemotherapy only. Four children received no treatment and treatment was unknown in 24 children.

The histology of recurrent SCT was mature teratoma in 117, immature teratoma in 34, and malignant teratoma in 126 children. The histology of recurrent SCT was unknown in 72 children. In 65 tumours (18.6%), there was a shift towards immaturity or malignancy.

Table 1

Patient characteristics for the total population and stratified per income countries.

	Total ($n=3407$)	High-income countries ($n=2296$)	Upper-middle income countries ($n=677$)	Lower-middle income countries ($n=377$)	Low-income countries ($n=57$)	*P*
Sex						
Male	844 (24.8%)	571 (24.9%)	161 (23.8%)	103 (27.3%)	9 (15.8%)	0.067
Female	2500 (73.4%)	1722 (75.0%)	491 (72.5%)	239 (63.4%)	48 (84.2%)	
Missing	63 (1.8%)	3 (0.1%)	25 (3.7%)	35 (9.3%)		
Median age at diagnosis, days	0 (0–54)	0 (0–17.5)	1 (0–108.5)	8 (0–150)	30 (2.5–556.5)	< 0.001
Altman classification						
I	1036 (30.4%)	669 (29.1%)	227 (33.5%)	125 (33.2%)	15 (26.3%)	< 0.001
II	1118 (32.8%)	753 (32.8%)	201 (29.7%)	137 (36.3%)	27 (47.4%)	
III	609 (17.9%)	407 (17.7%)	130 (19.2%)	63 (16.7%)	9 (15.8%)	
IV	548 (16.1%)	432 (18.8%)	851 (12.6%)	25 (6.6%)	6 (10.5%)	
Missing	96 (2.8%)	35 (1.5%)	34 (5.0%)	27 (7.2%)	–	
Median age at resection, days	13 (4–134.3)	9 (3–99)	17 (6–187.3)	40 (14–271.5)	52 (14.0–570)	< 0.001
Pathology						
Mature	2168 (63.7%)	1504 (65.5%)	442 (65.3%)	184 (48.8%)	38 (66.7%)	0.004
Immature	625 (18.3%)	469 (20.4%)	91 (13.4%)	54 (14.3%)	11 (19.3%)	
Malignant	366 (10.7%)	245 (10.7%)	91 (13.4%)	27 (7.2%)	3 (5.3%)	
Missing	248 (7.3%)	78 (3.4%)	53 (7.8%)	112 (29.7%)	5 (8.8%)	
Recurrence						
Yes	349 (10.2%)	254 (11.1%)	56 (8.3%)	33 (8.8%)	6 (12.3%)	0.604
No	2829 (83.0%)	1967 (85.7%)	536 (79.2%)	276 (73.2%)	50 (87.7%)	
Missing	229 (6.8%)	75 (3.3%)	85 (12.6%)	68 (18.0%)	1 (1.8%)	
Median time between primary resection and recurrence, days	348 (196–666)	348 (200.5–679)	358 (182.5–673.8)	357 (195.5–668)	311.5 (131.5–654.5)	0.948
Recurrence pathology						
Mature	117 (33.5%)	96 (37.8%)	14 (25.0%)	7 (21.2%)	–	0.001
Immature	34 (9.7%)	23 (9.1%)	4 (7.1%)	7 (21.2%)	–	
Malignant	126 (36.1%)	91 (35.8%)	22 (39.3%)	7 (21.2%)	6 (100%)	
Missing	72 (20.6%)	44 (17.3%)	16 (28.6%)	12 (36.4%)	–	
Outcome						
Alive	2876 (84.4%)	2073 (90.3%)	534 (78.9%)	219 (58.1%)	50 (87.7%)	0.059
Death	140 (4.1%)	93 (4.1%)	25 (3.7%)	20 (5.3%)	2 (3.5%)	
Missing	391 (11.5%)	130 (5.7%)	118 (17.4%)	138 (36.6%)	5 (8.8%)	

Data are *n* (%) or median (IQR).

**P* values represent univariable testing between country income strata.

Income country

In this global study, 62 countries participated. Table 1 shows the main patient characteristics per income group. SCT diagnosis and resection were later in LICs compared to LMICs, UMICs and HICs. The median age at diagnosis was 30 days (IQR 2.5–556.5) in LICs, 8 (0–150) in LMICs, 1 (0–108.5) UMICs, and 0 (0–17.5) in HICs ($P < 0.001$). The median age at resection was older: 52 days (IQR 14.0–570) in LICs compared to 40 (14–271.5), 17 (6–187.3), and 9 (3–99) days in LMICs, UMICs, and HICs, respectively ($P < 0.001$). Despite the earlier diagnosis and resection, a higher proportion of malignant SCTs at initial treatment was found in HICs ($n = 245$, 10.7%) and UMICs ($n = 91$, 13.4%) compared to LMICs ($n = 27$, 7.2%) and LICs ($n = 3$, 5.3%) ($P = 0.004$). The recurrence rates in all income groups were equivalent ($P = 0.604$).

Recurrence histology differed between groups with a malignancy percentage of 100% in LIC compared to 21.2, 39.3, and 35.8% in LMICs, UMICs, and HICs, respectively ($P = 0.001$). However, only six (12.2%) patients in LICs presented with recurrent SCT.

Factors associated with recurrent SCT

Logistic regression analysis with forward selection using the Wald statistics was used to determine factors associated with recurrent SCT. Sensitivity analysis with multiple imputation showed no effect of the imputed data on the multivariable outcomes. Therefore, missing data imputation was not done. The final models showed a good fit according to the Hosmer and Lemeshow test with a value of 0.993 and a Concordance Index of 0.655 with the following variables being associated with recurrent SCT: Altman type II (OR 1.62, 95% CI: 1.18–2.23), Altman type III (OR 1.63, 95% CI: 1.23–2.35), immature pathology of the initial tumour (OR 1.91, 95% CI: 1.43–2.56), and malignant pathology of the initial tumour (OR 4.0, 95% CI: 2.91–5.41). Income of countries ($P = 0.760$), age at diagnosis ($P = 0.254$), and age at resection ($P = 0.073$) were not associated with recurrence (Table 2).

Discussion

This global, retrospective study provides information about the treatment and outcome of 3407 patients with SCT in 62 countries.

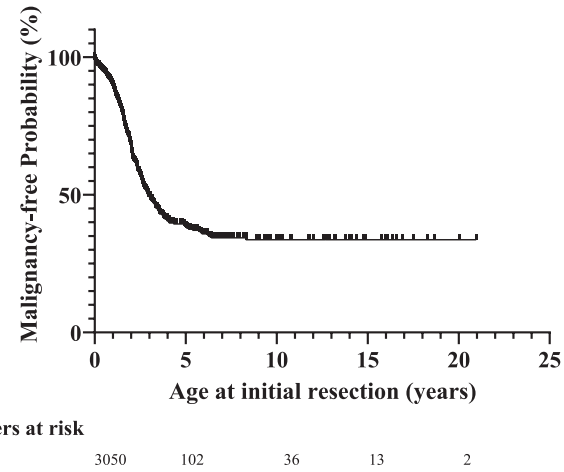

Figure 1. Malignancy-free probability at initial SCT resection.

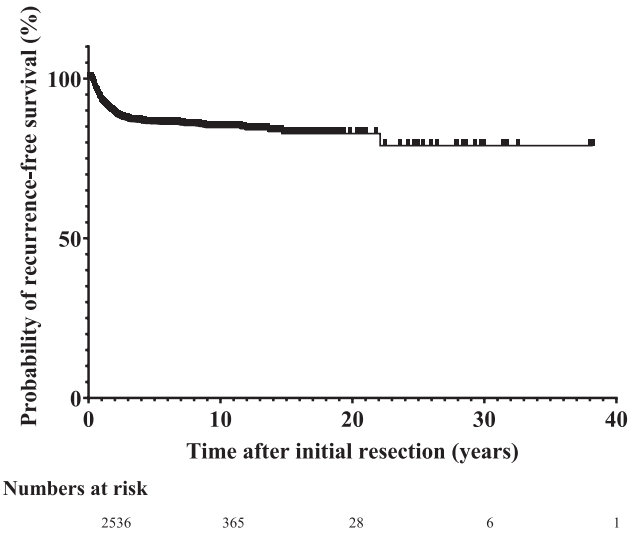

Figure 3. Probability of recurrence-free survival.

We found that the risk of initial malignant transformation increases with age, with a malignancy rate of ~30% after 2 years. After 6 years, the risk of initial malignant transformation stabilized at 64%. Furthermore, due to the increasing risk of malignant transformation, initial resection is preferably done at a young age. However, young neonates and infants are at higher risk of operative and postoperative complications[3]. In the current study, information about gestational age at birth or operative and postoperative complications has not been collected, which could influence the optimal time for resection.

Overall malignancy-free survival was 94.7% at age 1 year and 88.2% at 2 years. This was higher than reported by others with 80 and 58% of malignancy-free survival at age 1 and 2 years, respectively[15]. However, the latter study defined malignancy-free survival as time from birth to malignancy or death. In the present study, only deaths due to malignant disease were included in the survival analysis. Malignancy-free survival stabilized after the age of 6 years at 80%.

In this study, 349 (10.2%) children developed recurrence after a median period of 11.4 months after initial resection with late recurrences up to 22 years after initial resection. Others have also described occasional late recurrences up to 15 years after surgery[1]. There is no consensus about the duration of follow-up after SCT resection and recommendation varies from 3 to 6 years after resection[5,19]. In the current study, 96% of the recurrences were found within 5 years after initial resection including all malignant recurrences.

Factors associated with SCT recurrence were Altman type II or type III and initial immature or malignant histology, which has been previously documented[5]. Other risk factors for recurrence described by others included incomplete resection, no coccyx removal, and tumour spillage[5,20]. In the current study, data of these risk factors was not collected.

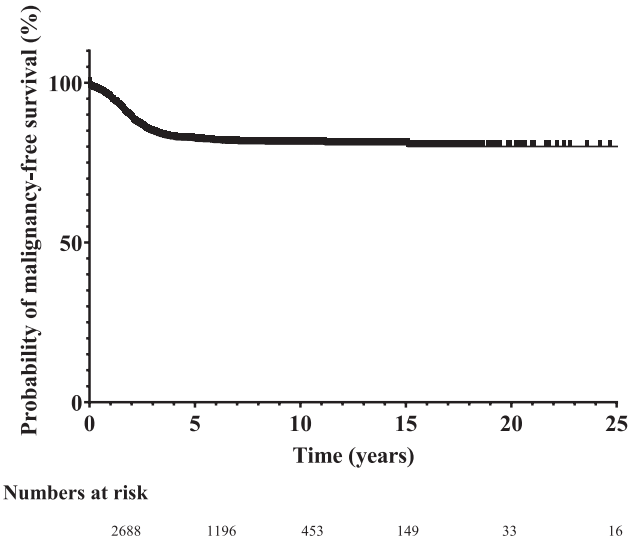

Figure 2. Probability of malignancy-free survival.

Income countries

Age at diagnosis and initial SCT resection were older in patients from LICs and LMICs compared to UMICs and HICs. This was also found in a recent study in children with retinoblastoma. This is probably due to late recognition and limited access to care[21]. In LIC Uganda only, it is estimated that only 15.2% of the Ugandan children with SCT presents in the hospital[22]. Moreover, the lack of paediatric intensive care facilities may force surgeons to postpone the SCT operation to an age with more physiological reserve.

In our study, the overall patient survival of children for all income countries was equivalent, which shows that SCT surgery can be done well and safely in LICs and LMICs. This is in contrast with others who found far better surgical outcomes for infants with other congenital disorders in HICs than in LICs or LMICs and found the income of the country as the greatest risk of mortality[11].

The difference with our study results may be explained by the very small and selected proportion of SCT patients who present for surgery in LICs and LMICs[22]. In many LICs and LMICs, patients with large tumours might have died without reaching the hospital due to cultural believes or inability to access paediatric surgical care. Evidence for this presumption comes from the fact that many centres invited to participate in the study declined because they never resected a SCT. Furthermore, the proportion

Table 2

Risk factors for recurrent SCT.

		Univariable		Multivariable	
	Recurrence rate	Odds ratio	*P*	Odds ratio	*P*
Altman classification					
I	73 of 1036	1			
II	122 of 1118	1.631 (1.203–2.211)	0.002*	1.624 (1.180–2.234)	0.003*
III	76 of 609	1.900 (1.353–2.668)	< 0.001*	1.627 (1.227–2.348)	0.009
IV	63 of 548	1.696 (1.189–2.419)	0.004	1.423 (0.967–2.093)	0.073
Income country					
Low	6 of 57	1			
Lower-middle	33 of 377	0.996 (0.397–2.502)	0.994		
Higher-middle	56 of 677	0.871 (0.357–2.121)	0.760		
High	254 of 2296	1.076 (0.457–2.535)	0.867		
Primary histology					
Mature	155 of 2168	1			
Immature	80 of 625	1.863 (1.3980–2.481)	< 0.001*	1.911 (1.427–2.558)	< 0.001*
Malignant	91 of 366	4.337 (3.245–5.795)	< 0.001*	3.965 (2.906–5.411)	< 0.001*
Median age at diagnosis (days)					
Yes	1 (0–248.3)				
No	0 (0-40)		0.254		
Median age at resection (days)					
Yes	17 (4–318)		0.073		
No	13 (4–120)				

of LICs and LMICs with a traditionally good healthcare system such as Syria, was relatively high in our study.

Many SCT patients who present in hospitals in LICs and LMICs do not receive components of neonatal surgical care that are considered essential in HICs. It is estimated that only half of the hospitals, with paediatric surgery in West African countries have neonatal ICU and many countries have fewer than one paediatric surgeon per million children[9,11,23–25].

Limitations

This study has several limitations such as its retrospective study design and long inclusion period. The incidence of SCT is very low, therefore, it would take a very long time before a similar prospective dataset could be obtained. Secondly, the number of collected variables was limited. This may have facilitated participation. Most variables could be obtained from electronic data files or patient letters. The percentage of missing data used in the analyses was, therefore, small, with a maximum percentage of 6.8%. Thirdly, the use of anonymized data made data validation not possible. On the other hand, this also may have reduced the risk of selection bias by not sharing data with an unfavourable outcome. Finally, there is bias because an unknown proportion of patients has not been included in the study. In an unknown but probably a relatively small number of patients in Western countries, the pregnancy of SCT patients is discontinued. Many SCT patients in LICs and LMICs do not receive any treatment.

Recommendations

We recommend complete resection of SCT before 1 month of age to minimise the risk of malignant transformation as long as it is safe and feasible. Furthermore, we advise to follow-up to 6 years of age since the vast majority of recurrences present within this timeframe. After this period, the chance of malignant transformation is probably small.

Conclusion

The United Nations encourages nations to create networks of experts for rare diseases and to increase support for research, by strengthening international collaboration and coordination of research efforts and the sharing of data, while respecting its protection and privacy[26]. We have shown that it is feasible to set up a large global study for a rare disease. The comprehensive study design herein and the large patient cohort enabled the identification of risk factors for recurrent SCT and essential information regarding malignant SCT transformation. With large, shared patient data sets, it is possible to answer important clinical questions that cannot be answered otherwise in order to improve the quality of care in every part of the world.

The SCT-study consortium

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Ethical approval

The Medical Ethical Board of Amsterdam University Medical Centre (Amsterdam UMC), determined that Medical Research Involving Human Subject Act (WMO) does not apply to the study and that official approval of the committee was not required (reference number W19_329 # 19.388).

Consent

Individual patient written consent was not obtained since the study included patients with intrauterine and neonatal death. Patient data collection was fully anonymous and cannot be traced back to the individual patient. The absence of written consent was discussed with the Medical Ethical Board.

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Author contribution

L.W.E.v.H.: gained study funding, wrote the study protocol, and established the SCT-study consortium; L.J.v.H.: designed the data collection forms, coordinated the data collection and validation, undertook the data analysis, and wrote and revised the manuscript; the writing committee (J.H.A., M.M.B., L.B.C., J.P. M.D., S.F., N.J.H., A.H., L.J.v.H., L.W.E.v.H., T.S., S.StP., J.T., and T.Y.) contributed to the data interpretation, manuscript content, and revisions; L.J.v.H. and J.T.: statistical analysis; L.W. E.v.H., L.J.v.H., J.P.M.D., and statistician (J.T.) had full access to all the study data; L.J.v.H. and statistician (J.T.) validated the data. All authors (SCT-study group) approved the manuscript and had final responsibility for the decision to submit for publication. All authors were local investigators. Local investigators gained local study approval, used the protocol to identify eligible patients, collected data, entered data in Castor EDC, and checked the data to prevent duplicate entries and ensure accuracy. All authors have read and approved the final manuscript.

Conflicts of interest disclosure

All authors declare no conflicts of interest

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Guarantor

L.W.E. van Heurn, J.P.M. Derikx, and L.J. van Heurn are guarantors for this study.

Data availability statement

Following publication of the study results, the full, anonymous de-identified patient dataset will be made available. Data requestors will need to sign a data access agreement.

Provenance and peer review

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References

[1] Padilla BE, Vu L, Lee H, *et al*. Sacrococcygeal teratoma: late recurrence warrants long-term surveillance. Pediatr Surg Int 2017;33:1189–94.
[2] De Backer A, Madern GC, Hakvoort-Cammel FG, *et al*. Study of the factors associated with recurrence in children with sacrococcygeal teratoma. J Pediatr Surg 2006;41:173–81; discussion 173-81.
[3] Michelet D, Brasher C, Kaddour HB, *et al*. Postoperative complications following neonatal and infant surgery: common events and predictive factors. Anaesth Crit Care Pain Med 2017;36:163–9.
[4] De CF, Sarnacki S, Patte C, *et al*. Prognosis of malignant sacrococcygeal germ cell tumours according to their natural history and surgical management. Surg Oncol 2012;21:e31–7.
[5] Derikx JP, De BA, van de Schoot L, *et al*. Factors associated with recurrence and metastasis in sacrococcygeal teratoma. Br J Surg 2006;93: 1543–8.
[6] Wang Y, Wu Y, Wang L, *et al*. Analysis of recurrent sacrococcygeal teratoma in children: clinical features, relapse risks, and anorectal functional sequelae. Med Sci Monit 2017;23:17–23.
[7] Pauniaho SL, Tatti O, Lahdenne P, *et al*. Tumor markers AFP, CA 125, and CA 19-9 in the long-term follow-up of sacrococcygeal teratomas in infancy and childhood. Tumour Biol 2010;31:261–5.
[8] Yao W, Li K, Zheng S, *et al*. Analysis of recurrence risks for sacrococcygeal teratoma in children. J Pediatr Surg 2014;49:1839–42.
[9] Chirdan LB, Uba AF, Pam SD, *et al*. Sacrococcygeal teratoma: clinical characteristics and long-term outcome in Nigerian children. Ann Afr Med 2009;8:105–9.
[10] Abubakar AM, Nggada HA, Chinda JY. Sacrococcygeal teratoma in Northeastern Nigeria: 18-years experience. Pediatr Surg Int 2005;21:645–8.
[11] Global PaedSurg Research Collaboration. Mortality from gastrointestinal congenital anomalies at 264 hospitals in 74 low-income, middle-income, and high-income countries: a multicentre, international, prospective cohort study. Lancet 2021;398:325–39.
[12] von Elm E, Altman DG, Egger M, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–9.
[13] Mathew G, Agha R, Albrecht J, *et al*. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case–control studies in surgery. Int J Surg 2021;96:106165.
[14] Currarino G, Coln D, Votteler T. Triad of anorectal, sacral, and presacral anomalies. Am J Roentgenol 1981;137:395–8.
[15] Dirix M, van Becelaere T, Berkenbosch L, *et al*. Malignant transformation in sacrococcygeal teratoma and in presacral teratoma associated with Currarino syndrome: a comparative study. J Pediatr Surg 2015;50:462–4.
[16] Castor Electronic Data Capture. Castor Electronic Data Capture 2019 [27 August 2019], https://castoredc.com
[17] Altman RP, Randolph JG, Lilly JR. Sacrococcygeal teratoma: American Academy of Pediatrics Surgical Section Survey-1973. J Pediatr Surg 1974; 9:389–98.
[18] Hamadeh NRv, C. Metreau E. New World Bank country classifications by income level: 2022-2023; 2022. https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023
[19] Kops AL, Hulsker CC, Fiocco M, *et al*. Malignant recurrence after mature Sacrococcygeal teratoma: a meta-analysis and review of the literature. Crit Rev Oncol Hematol 2020;156:103140.
[20] De BA, Madern GC, Hakvoort-Cammel FG, *et al*. Study of the factors associated with recurrence in children with sacrococcygeal teratoma. J Pediatr Surg 2006;41:173–81.
[21] Fabian ID, Abdallah E, Abdullahi SU. Global retinoblastoma presentation and analysis by national income level. JAMA Oncol 2020;6: 685–95.
[22] Badrinath R, Kakembo N, Kisa P, *et al*. Outcomes and unmet need for neonatal surgery in a resource-limited environment: estimates of global health disparities from Kampala, Uganda. J Pediatr Surg 2014;49:1825–30.
[23] Chirdan LB, Ameh EA, Abantanga FA, *et al*. Challenges of training and delivery of pediatric surgical services in Africa. J Pediatr Surg 2010;45: 610–8.
[24] Okoye MT, Ameh EA, Kushner AL, *et al*. A pilot survey of pediatric surgical capacity in West Africa. World J Surg 2015;39:669–76.
[25] Sitkin NA, Ozgediz D, Donkor P, *et al*. Congenital anomalies in low- and middle-income countries: the unborn child of global surgery. World J Surg 2015;39:36–40.
[26] United Nations. Addressing the challenges of persons living with a rare disease and their families - Resolution adopted by the General Assembly on 16 December 2021; 2022. https://www.rarediseasesinternational.org/wp-content/uploads/2022/01/Final-UN-Text-UN-Resolution-on-Persons-Living-with-a-Rare-Disease-and-their-Families.pdf