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Japanese Clinical Practice Guidelines for Sacrococcygeal Teratoma, 2017

(Running title: Guidelines for sacrococcygeal teratoma)

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Guideline

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Abstract

Background: Sacrococcygeal teratoma (SCT) is the most common extragonadal germ cell tumor in neonates and infants. Although most cases of infantile SCT are benign tumors by nature, some develop into extremely large lesions, leading to massive bleeding, high-output heart failure, disseminated intravascular coagulation, and even fatal outcomes during the neonatal period. In addition, some cases may present with tumor recurrence, malignant transformation, long-term sequelae (including bladder and bowel dysfunction) and lower leg palsy during the long-term follow-up. However, SCT is very rare, and there are few opportunities to encounter this disease, so general physicians without expert credentials currently lack information relevant to clinical practice. That is why our research project committee has compiled guidelines concerning SCT.

Methods: The purpose of these guidelines was to share information concerning the treatment and follow-up of infantile SCT. The guidelines were developed using the methodologies in the Medical Information Network Distribution System. A comprehensive search of the Japanese and English articles in PubMed and Ichu-Shi Web revealed only case reports or case series, and the recommendations were developed through a process of informal consensus.

Results: The clinical questions addressed the risk factors, the efficacy of Caesarean section, the initial devascularization of tumor feeding vessels, interventional radiology, recommended clinical studies for follow-up and possible long-term complications.

Conclusions: These are the first guidelines for SCTs to be established in Japan, and they may have huge clinical value and significance in terms of developing therapeutic strategies and follow-up, potentially contributing to the improvement of the prognosis and quality of life of SCT patients.

Outline of the disorder and the background concerning the development of the guidelines

Sacrococcygeal teratoma (SCT) is the most common extragonadal germ cell tumor in neonates and infants. This lesion consists of a solid and/or cystic component and develops either from the tip of the sacrum, protruding outward from the buttocks, or within the pelvic cavity. SCT occurs in 1 out of every 40,000 births, and the male-female ratio is approximately 1:3, more frequently occurring in girls. Although most cases diagnosed at the time of birth are mature/immature teratomas, yolk sac tumors occur more frequently in children after 1 year of age, reportedly occurring at a rate of ≥75% [1].

The Altman classification is commonly used for classification according to the occurrence site of SCT and includes the following types: Type I, most of the tumor constitutes components outside the pelvis; Type II, although there is development inside the pelvic cavity, the components outside the pelvis are larger; Type III, although there is development outside the pelvis, the components inside the pelvic cavity and abdomen are larger; Type IV, there is no development outside the pelvis, only including components inside the pelvic cavity and abdomen.

As for treatment of SCT, surgical excision is carried out for mature and immature teratomas. In cases of Altman type I, many patients undergo surgery approaching from the buttocks, while laparostomy is concomitantly used in patients with large amounts of intraabdominal components. With gigantic solid masses, the risk of bleeding is high, and ligation of the median sacral artery first, which is a nutrient blood vessel, may be useful. With yolk sac tumors, chemotherapy, such as BEP therapy, may be carried out first, followed by surgical excision.

Although most cases of infantile SCT are benign tumors by nature, some develop into extremely large ones, leading to massive bleeding, high-output heart failure and disseminated intravascular coagulopathy (DIC), and fatal outcomes during the neonatal period can occur as well.

In addition, even after successful tumor excision, some cases may present with tumor recurrence, malignant transformation, bladder and bowel dysfunction as well as lower-leg palsy during long-term follow-up.

No clear medical guidelines for SCT have yet been established because SCT is very rare and there are few opportunities to encounter this disease, not only for pediatricians and obstetricians but also for pediatric surgeons. Therefore, there is insufficient information concerning the risk factors of severity, optimal mode of delivery, treatment strategies and appropriate follow-up assessment for general physicians without expert credentials.

Our research project committee has compiled a set of guidelines furnishing information about SCT to clinicians to help improve the prognosis and quality of life (QOL) of this disease. The essence of the newly proposed Japanese clinical guidelines for SCT is summarized in this report.

Methods of formulating the guidelines

The purpose of these guidelines was to share information on the disease concept, diagnostic criteria and severity assessment as well as to assist in making decisions in the prenatal management, treatment and follow-up for patient's families and general physicians, including obstetricians, neonatologists, pediatricians and pediatric surgeons.

Coverage of the clinical practice guidelines was as follows: (1) SCTs in infants and young children; (2) treatment for patients who have been definitively diagnosed with this disease; (3) the prenatal diagnosis, perinatal care management, preoperative management, interventional radiology (IVR), surgical therapy and postoperative management; and (4) complications, long-term follow-up and the prognosis.

The guidelines were developed using the methodologies described in the Medical Information Network Distribution System (Minds) Handbook for Clinical Practice Guideline Development 2014 [2] and the Minds Manual for Clinical Practice Guideline Development [3]. The panel of experts consisted of obstetricians, neonatologists, pediatricians, radiologists and pediatric surgeons. The members met several times in person to discuss evidence from a systematic review and draft recommendations. Panel members and their fields of expertise are listed in Table 1.

The English literature search was conducted by The MEDLINE database via PubMed (until September 2014). Japanese literature was collected from the Internet version of the Japana Centra Revuo Medicina (Nippon Igaku Chuuou Zasshi; until September 2014). A total of 1388 papers were collected. First, the titles and abstracts of all papers were examined, and 354 important papers were chosen for a further examination of their full texts. Each paper was independently evaluated by two examiners. Finally, 105 articles were reviewed systematically by 7 members of the

systematic review (SR) team. The guideline development group created the recommendations and commentary based on the materials submitted by the SR team.

During screening, there were no Cochrane reviews, SRs, randomized controlled trials, nonrandomized controlled trials, interventional studies or observational research, and all of the articles were case reports or case series, with no references adopted for the evaluation of the body of evidence. For this reason, we feel that a qualitative review was conducted, and we reached decisions through a process of informal consensus involving a group discussion process designed to allow all members of the group to voice their opinions and contribute equally to the decision-making with the goal of providing recommendations that would be useful for clinical practice [4].

Finally, the guidelines consisted of 6 clinical questions (CQs) and recommendations to these questions related to the assessment of the severity, prenatal management, treatment, follow-up and possible long-term complications (Fig 1). The guidelines merely offer standards of management and are not necessarily meant to regulate clinical practice.

Recommendations

CQ1: What are the risk factors related to the vital prognosis of sacrococcygeal teratoma?

Recommendation: Risk factors related to the vital prognosis of sacrococcygeal teratomas reportedly include the tumor size and growth rate, tumor histological and component type, complications of fetal edema and heart failure and early delivery. Attention should be paid to the existence of these risk factors when planning treatment for sacrococcygeal teratomas.

Risks related to the vital prognosis can be divided into tumor-related and patient-related factors. The tumor size and growth rate as well as its histological (mature/immature) and component type (solid/cystic/mixed) may be risk factors of tumors related to the vital prognosis [5-15]. In contrast, as risk factors among children, heart failure and fetal edema have been well reported to be related to mortality [16-17]. Usui et al. reported that the mortality rates among patients with a gestational age of <28 weeks, 28 to 31 weeks, 32 to 36 weeks, and ≥37 weeks were respectively 60%, 38%, 11% and 0% [10]. We therefore assume that fetal edema, heart failure and early delivery may be risk factors in children related to the vital prognosis.

CQ2: Does Caesarean section improve the prognosis of tumors with extrapelvic lesions?

Recommendation: For tumor lesions outside the pelvis, it is reasonable to consider Caesarean section depending on the size thereof in order to avoid tumor rupture, tumor hemorrhaging and delivery difficulty.

While there are no reports comparing Caesarean delivery and vaginal delivery with respect to the vital prognosis, several studies have reported problems with vaginal delivery due to SCTs.

These problems include the fact that extrapelvic lesions cause fetal malposition or hinder the progress of labor, along with the fact that the tumors may rupture at delivery, leading to bleeding of the tumor and blood loss in the fetus [18-22]. However, some reports suggested that vaginal delivery is considered depending on the tumor size (less than 5 cm) [15,23]. The delivery-related factor having the greatest impact on the prognosis of the fetus is blood loss due to tumor damage, and Caesarean section delivery may potentially reduce such risks.

Regarding comparisons between scheduled Caesarean section and emergency Caesarean section, Japanese papers reported that the proportion of emergency procedures was significantly higher in cases of postnatal death than in surviving cases (72.7% vs. 29.9%), while that of scheduled procedures was significantly lower (18.2% vs. 48.1%) [15]. It may be necessary to perform appropriate medical intervention before emergency Caesarean sections is required.

In summary, when Caesarean section is performed at an appropriate time for extrapelvic tumor lesions, it may reduce the risk of tumor rupture and bleeding and improve the prognosis, especially in large tumors. However, the vital prognosis is affected by many other factors, making it hard to conclude that it can be improved by Caesarean section alone.

CQ3: In the surgical treatment of sacrococcygeal teratomas, is the initial devascularization of tumor feeding vessels effective?

Recommendation: For sacrococcygeal teratomas with hypervascularity, the initial devascularization of feeding vessels originating from the median sacral artery and the internal iliac artery may be considered.

There have been many reports indicating that the devascularization of feeding vessels from the median sacral artery or the internal iliac artery prior to tumor resection was useful for decreasing the intraoperative amount of bleeding. As methods of devascularization, there have been reports of ligation by laparotomy [24-28] as well as that using laparoscopy [29-32]. However, despite the pretreatment of feeding blood vessels, some reports have indicated that massive bleeding was observed during surgery, and pretreatment was not effective [27, 33]. There have been no reports on complications related to the intraperitoneal pretreatment of tumor-feeding vessels, including postoperative ileus, nor have there been any reports on the improvement of the vital prognosis or reduction in the rate of postoperative complications due to pretreatment. With respect to the amount of bleeding, the number of reports indicating the effectiveness and benefit of pretreatment exceeded that of reports showing the ineffectiveness thereof, with no reports indicating any harm caused by pretreatment. Therefore, we concluded that the pretreatment of feeding vessels from the median sacral artery or the internal iliac artery may be effective and should be considered.

CQ4: Is IVR useful as an adjunctive treatment?

Recommendation: Although IVR for sacrococcygeal teratomas facilitates tumor removal and may reduce the amount of bleeding at the time of removal, there have been few cases performed, and a skilled technique is required for the procedure. Therefore, we recommend that the feasibility of the procedure at each facility be thoroughly examined before its application.

The four cases of IVR performed in neonates with SCT were all transcatheter arterial embolization [34-37], including one case in which radiofrequency ablation (RFA) was carried out

prior to birth [35], and one case in which RFA was performed as an additional treatment after embolization [34]. The maximum diameter of all tumors subjected to such treatment was ≥10 cm. In two cases, it was reported that although IVR is effective, proficient skill is required for the procedure [34,36].

While there were no reports on the improvement of the vital prognosis, all cases that underwent IVR survived, and the tumor was able to be easily removed in two cases [36,37]. However, persistent blood transfusion and hyperkalemia caused difficulty in intraoperative management with intraoperative cardiac arrest in one case [36]. During subsequent tumor resection, there was little bleeding in three of four cases. The reduction in the rate of postoperative complications was unclear, and no reports described complications occurring after surgery. None of the four cases of IVR described the complications associated therewith.

CQ5: What kinds of clinical studies are recommended for follow-up of recurrence after treatment?

Recommendations: While the risk of recurrence of malignant teratomas is high, it should be noted that even mature or immature teratomas may develop malignant recurrence. AFP measurements are recommended for the early detection of malignant recurrence. It is necessary to conduct follow-ups for three years after the end of treatment.

There were no prospective clinical studies on the recurrence of sacrococcygeal teratomas during this study period. According to several retrospective reports, the recurrence rate was 8.9% in the Netherlands [38] and 8.3% in Japan [12]. In the MAKEI study, the time to recurrence with malignant transformation of neonatal SCTs was reportedly 12 to 26 months [39]. Recurrence risk

factors include malignant teratomas and positivity for resection stumps in malignant cases. Even mature or immature teratomas with complete resection may recur with malignant transformation, underscoring the need to perform follow-up until three years of age, as most cases of recurrence occur by the age of two [12,13,38-41].

There have been many reports on the measurement of alfa fetoprotein (AFP) at follow-up for recurrence, many of which indicate high AFP levels at the onset. According to Hawkins et al. (POG/CCSG) [41], AFP was increased in all 6 patients (100%) with recurrent malignant SCTs (218 to 32,000 ng/mL), and according to Schneider et al. (MAKEI) [39], AFP was increased in 21 of 22 patients (95.4%) with recurrent malignant SCTs. In addition, Pauniaho et al. reported a high level of AFP (2.5-fold the median) in 33% of non-recurrent patients (6/18), with a high level of AFP in 66% of recurrent patients (4/6) [42]. These facts suggest that AFP may be useful for the follow-up of recurrence.

CQ6: What long-term complications might occur after treatment?

Recommendations: In newborns and infants with SCTs, long-term complications, including an impaired bowel function and/or urinary incontinence, lower leg palsy and cosmetically unacceptable scarring, often occur, even in cases with complete removal. It is recommended to mention these facts to patients/families before deciding on the course of treatment.

For neonates and infants with SCTs, severe long-term complications after curative surgery may significantly reduce the QOL. Therefore, it is important to recognize these long-term complications and ensure they are taken care of through follow-ups and adjustments to their home life. Several references suggest the following five items to be major long-term sequelae: 1) an

impaired bowel function, 2) urinary incontinence, 3) lower leg palsy, 4) sexual dysfunction and 5) cosmetically unacceptable scarring.

An impaired bowel function and urinary incontinence are common long-term complications after surgery for SCTs. The occurrence of such complications range from 19%-38% for bowel function and around 50% for urinary incontinence, with both occurring in 11%-45.2% of cases [43-46]. Reported risk factors include obstruction of the urinary tract and intestinal tract at the prenatal imaging diagnosis, tumor recurrence, types other than Altman type I and abdominosacroperineal resection for Altman type III and IV [45,46]. However, Cozzi et al. reported that there was no significant difference between adult patients with SCTs and the control group [47].

Impaired movement of the lower leg has been reported in 5.0%-11.1% of cases [48-51]. However, there has been little description of the extent of such impairment. Likewise, there are few documents on the sexual function of these patients. Regarding trouble during sexual intercourse, Draper et al. reported that some women were incapable of sexual intercourse due to pain while some men had impotence [52], and another study reported that 20% of men had impotence while 10% of women experienced urinary incontinence during sexual intercourse [49]. Regarding pregnancy and delivery, 38.5% of patients were able to have children on their own [49]. According to a report in a Scottish national cohort [43], 22.2% of women over 16 years of age had gone through pregnancy and given birth.

Regarding cosmetically unacceptable scarring, 40.3% of patients with SCT complained that their surgical wounds were unacceptable, with a significant difference between patients diagnosed prior to eight years of age and those with large tumors, according to Derikx et al. [44].

Based on the above reports, after surgery for SCT, patients may suffer from an impaired bowel function and/or urinary incontinence, lower leg palsy and cosmetically unacceptable scarring, indicating the importance of conducting follow-ups while taking these facts into consideration.

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The English used in this manuscript was reviewed by Brian Quinn (President, Medical English Service).

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

[1] Rescorla FJ. Teratomas and other germ cell tumors. In: Coran AG, Adzick NS, Krummel TM, Laberge JM, Shmberger RC, Caldamone AA (eds). *Pediatric Surgery 7th ed*. Elsevier Saunders, Philadelphia, 2012; 947-57.

[2] Fukui T, Yamaguchi N. *Medical Information Network Distribution System Handbook for Formulating Clinical Practice Guidelines 2014.* Igaku-shoin, Tokyo, 2014 (in Japanese).

[3] Morizane T, Yoshida M. *Minds Manual for Guideline Development 1st ed.* Japan Council for Quality Health Care, Tokyo, 2014 (in Japanse).

[4] World Health Organization. *WHO handbook for guideline development 2nd ed.* World Health Organization, 2014.

[5] Brace V, Grant SR, Brackley KJ, et al. Prenatal diagnosis and outcome in sacrococcygeal teratomas: a review of cases between 1992 and 1998. *Prenat Diagn.* 2000; 20: 51-5.

[6] Wilson RD, Hedrick H, Flake AW, et al. Sacrococcygeal teratomas: prenatal surveillance, growth and pregnancy outcome. *Fetal Diagn Ther.* 2009; 25: 15-20.

[7] Shue E, Bolouri M, Jelin EB, et al. Tumor metrics and morphology predict poor prognosis in prenatally diagnosed sacrococcygeal teratoma: a 25-year experience at a single institution. *J Pediatr Surg.* 2013; 48: 1225-31.

[8] Rodriguez MA, Cass DL, Lazar DA, et al. Tumor volume to fetal weight ratio as an early prognostic classification for fetal sacrococcygeal teratoma. *J Pediatr Surg.* 2011; 46: 1182-5.

[9] Benachi A, Durin L, Vasseur Maurer S, et al. Prenatally diagnosed sacrococcygeal teratoma: a prognostic classification. *J Pediatr Surg.* 2006; 41: 1517-21.

[10] Usui N, Kitano Y, Sago H, et al. Outcomes of prenatally diagnosed sacrococcygeal teratomas: the results of a Japanese nationwide survey. *J Pediatr Surg.* 2012; 47: 441-7.

[11] Perrelli L, D'Urzo C, Manzoni C, et al. Sacrococcygeal teratoma. Outcome and management. An analysis of 17 cases. *J Perinat Med.* 2002; 30: 179-84.

[12] Yoneda A, Usui N, Taguchi T, et al. Impact of the histological type on the prognosis of patients with prenatally diagnosed sacrococcygeal teratomas: the results of a nationwide Japanese survey. *Pediatr Surg Int*. 2013; 29: 1119-25.

[13] 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.

[14] Addeo R, Crisci S, D'Angelo V, et al. Bax mutation and overexpression inversely correlate with immature phenotype and prognosis of childhood germ cell tumors. *Oncol Rep.* 2007; 17: 1155-61.

[15] Kanamori Y, Usui N, Kitano Y, et al. Analysis of dead cases who were antenatally diagnosed as sacrococcygeal teratoma -from Japanese nationwide survey-. *Japanese Journal of Pediatric Surgery.* 2012; 48: 834-39 (in Japanese).

[16] Okada T, Sasaki F, Cho K, et al. Management and outcome in prenatally diagnosed sacrococcygeal teratomas. *Pediatr Int.* 2008; 50: 576-80.

[17] Hedrick HL, Flake AW, Crombleholme TM, et al. Sacrococcygeal teratoma: prenatal assessment, fetal intervention, and outcome. *J Pediatr Surg.* 2004; 39: 430-8.

[18] Holzgreve W, Mahony BS, Glick PL, et al. Sonographic demonstration of fetal sacrococcygeal teratoma. *Prenatl Diagn.* 1985; 5: 245-57.

[19] Flake AW, Harrison MR, Adzich NS, et al. Fetal sacrococcygeal teratoma. *J Pediatr Surg.* 1986; 21: 563-6.

[20] Holzgreve W, Miny P, Anderon R, et al. Experience with 8 cases of prenatally diagnosed sacrococcygeal teratomas. *Fetal Ther.* 1987; 2: 88-94.

[21] Sepulveda WH. Prenatal sonographic diagnosis of congenital sacrococcygeal teratoma and management. *J Perinat Med.* 1989; 17: 93-7.

[22] Uchiyama M, Iwafuchi M, Yagi M, et al. Sacrococcygeal teratoma; a series of 19 cases with long-term follow-up. *Eur J Pediatr Surg.* 1999; 9: 158-62.

[23] Gross SJ, Benzie RJ, Sermer M, et al. Sacrococcygeal teratoma: prenatal diagnosis and management. *Am J Obstet Gynecol.* 1987; 156: 393-6.

[24] Lindahl BH. Giant sacrococcygeal teratoma: a method of simple intraoperative control of hemorrhage. *J Pediatr Surg.* 1988; 23: 1068-9.

[25] Robertson, FM, Crombleholme, TM, Frantz III ID, et al. Devascularization and staged resection of giant sacrococcygeal teratoma in the premature infant. *J Pediatr Surg.* 1995; 30: 309-11.

[26] Angel CA, Murillo C, Mayhew J. Experience with vascular control before excision of giant, highly vascular sacrococcygeal teratomas in neonates. *J Pediatr Surg.* 1998; 33: 1840-2.

[27] Kamata S, Imura K, Kubota A, et al: Operative management for sacrococcygeal teratoma diagnosed in utero. *J Pediatr Surg.* 2001; 36: 545-8.

[28] Uemura S, Choda Y, Yoshida A, Nakagawa Y. Intraoperative vascular control using aortic snare before excision of giant sacrococcygeal teratoma. *Jpn J Pediatr Surg.* 2002; 34: 1438-41 (in Japanese).

[29] Bax NMA, van der Zee DC. Laparoscopic clipping of the median sacral artery in huge sacrococcygeal teratomas. *Surg Endosc.* 1998; 12: 882-3.

[30] Lukish JR, Powell DM. Laparoscopic ligation of the median sacral artery before resection of a sacrococcygeal teratoma. *J Pediatr Surg.* 2004; 39: 1288-90.

[31] Solari V, Jawaid W, Jesudason EC, et al. Enhancing safety of laparoscopic vascular control for neonatal sacrococcygeal teratoma. *J Pediatr Surg.* 2011; 45: E5-E7.

[32] Takehara H, Kuyama H. Laparoscopic-assisted resection to the intrapelvic and intra-abdominal component of sacrococcygeal teratoma – A case report. *Jpn J Pediatr Surg.* 2009; 41: 987-91 (in Japanese).

[33] Kaneyama K, Yamataka A, Kobayashi H, et al: Giant, highly vascular sacrococcygeal teratoma: report of its excision using the ligasure vessel sealing system. *J Pediatr Surg.* 2004; 39: 1971-3.

[34] Cowles RA, Stolar CJH, Kandel JJ, et al. Preoperative angiography with embolization and radiofrequency ablation as novel adjuncts to safe surgical resection of a large, vascular sacrococcygeal teratoma. *Pediatr Surg Int.* 2006; 22: 554-6.

[35] Tanaka H, Takayasu H, Fujino A, et al. Perinatal management and neonatal surgery for giant sacrococcygeal teratoma. *Jpn J Pediatr Surg.* 2008; 40: 823-8 (in Japanese).

[36] Lahdes-Vasama TT, Korhonen PH, Seppanen JM, et al. Preoperative embolization of giant sacrococcygeal teratoma in a premature newborn. *J Pediatr Surg.* 2011; 46: E5-8.

[37] Rossi UG, Cariati M, Toma P. Giant sacrococcygeal teratoma embolization. *Indian J Radiol Imaging.* 2013; 23: 145-7.

[38] Derikx JP, De Backer A, van de Schoot L, et al. Factors associated with recurrence and metastasis in sacrococcygeal teratoma. *Br J Surg.* 2006; 93: 1543-8.

[39] Schneider DT, Wessalowski R, Calaminus G, et al. Treatment of recurrent malignant sacrococcygeal germ cell tumors: analysis of 22 patients registered in the German protocols MAKEI 83/86, 89, and 96. *J Clin Oncol.* 2001; 19: 1951-60.

[40] Rescorla FJ, Sawin RS, Coran AG, et al. Long-term outcome for infants and children with sacrococcygeal teratoma: a report from the Childrens Cancer Group. *J Pediatr Surg.* 1998; 33: 171-6.

[41] Hawkins E, Issacs H, Cushing B, et al. Occult malignancy in neonatal sacrococcygeal teratomas. A report from a Combined Pediatric Oncology Group and Children's Cancer Group study. Am *J Pediatr Hematol Oncol.* 1993; 15: 406-9.

[42] 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. *Tumor Biol.* 2010; 31: 261–5.

[43] Shalaby MS, Walker G, O'Toole S, et al. The long-term outcome of patients diagnosed with sacrococcygeal teratoma in childhood. A study of a national cohort. *Arch Dis Child.* 2014; 99: 1009-13.

[44] Derikx JP, De Backer A, van de Schoot L, et al: Long-term functional sequelae of sacrococcygeal teratoma: a national study in The Netherlands. *J Pediatr Surg.* 2007; 42: 1122-6.

[45] Partridge EA, Canning D, Long C, et al. Urologic and anorectal complications of sacrococcygeal teratomas: prenatal and postnatal predictors. *J Pediatr Surg.* 2014; 49: 139-42.

[46] Barakat MI, Abdelaal SM, Saleh AM. Sacrococcygeal teratoma in infants and children. *Acta Neurochir (Wien).* 2011; 153: 1781-6.

[47] Cozzi F, Schiavetti A, Zani A, et al. The functional sequelae of sacrococcygeal teratoma: a longitudinal and cross-sectional follow-up study. *J Pediatr Surg.* 2008; 43: 658-61.

[48] Lee MY, Won HS, Hyun MK, et al. Perinatal outcome of sacrococcygeal teratoma. *Prenat Diagn.* 2011; 31: 1217-21.

[49] Rintala R, Lahdenne P, Lindahl H, et al. Anorectal function in adults operated for a benign sacrococcygeal teratoma. *J Pediatr Surg.* 1993; 28: 1165-7.

[50] Malone PS, Spitz L, Kiely EM, et al. The functional sequelae of sacrococcygeal teratoma. *J Pediatr Surg.* 1990; 25: 679-80.

[51] Zaccara A, Iacobelli BD, Adorisio O, et al. Gait analysis in patients operated on for sacrococcygeal teratoma. *J Pediatr Surg.* 2004; 39: 947-52.

[52] Draper H, Chitayat D, Ein SH, et al. Long-term functional results following resection of neonatal sacrococcygeal teratoma. *Pediatr Surg Int.* 2009; 25: 243-6.

Table

Table 1. Panel of experts compiling the guidelines

Guideline development team

No.	Name	Certifiation	Affiliation
1	Tajiri Tatsuro (chairman)	Board-certified pedatric surgeon	Department of Pediatric Surgery, Kyoto Prefectural University of Medicine
2	Noriaki Usui (vice chairman)	Board-certified pedatric surgeon	Department of Pediatric Surgery, Osaka Women's and Children's Hospital
3	Masanori Tamura	Board-certified neonatalogist	Department of Pediatrics, Saitama Medical Center, Saitama Medical University
4	Haruhiko Sago	Board-certified obstetrician	Department of Maternal-Fetal and Neonatal Medicine, National Center for Child Health and Development
5	Shigeru Ono	Board-certified pedatric surgeon	Department of Pediatric Surgery, Jichi Children's Medical Center Tochigi, Jichi Medical University
6	Shunsuke Nosaka	Board-certified radiologist	Division of Radiology, National Center for Child Health and Development

Systematic review team

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5	Kohei Sakai	Board-certified pedatric surgeon	Department of Pediatric Surgery, Kyoto Prefectural University of Medicine
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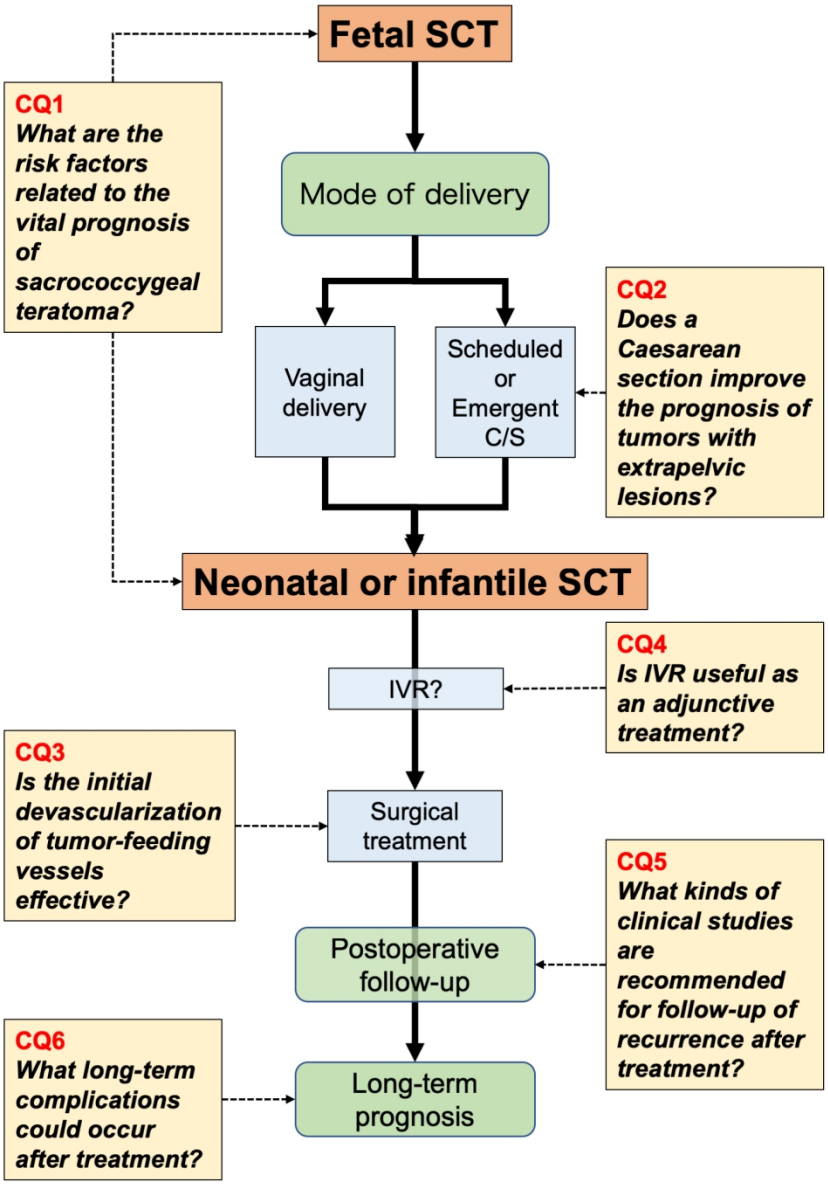
7	Takahiro Sugiura	Board-certified pedatrician	Department of Pediatrics, Toyohashi Municipal Hospital

Figure Legends

Fig. 1. A flowchart concerning the management of infantile sacrococcygeal teratoma. SCT, sacrococcygeal teratoma; C/S, Caesarean section; IVR, interventional radiology.



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