RESEARCH ARTICLE

Soft-tissue Sarcomas in the Asia-Pacific Region: A Systematic Review

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Abstract

 <u>Background</u>: **Soft-tissue sarcomas require tailored and multidisciplinary treatment and management. However, little is known about how sarcomas are treated and managed throughout the Asia-Pacific region. <u>Materials and Methods</u>: MEDLINE was systematically searched using prespecified criteria. Publications (previous 10 years) that reported tumour characteristics, treatment patterns, survival outcomes, and/or safety outcomes of patients with soft-tissue sarcoma were selected. Exclusion criteria were studies of patients <18 years of age; ≤10 patients; countries other than Australia, Hong Kong, Indonesia, Korea, Malaysia, New Zealand, Philippines, Singapore, Taiwan, or Thailand; >20% benign tumours; sarcomas located in bones or joints; gastrointestinal stromal tumour; Kaposi's sarcoma; or not reporting relevant outcomes. <u>Results:</u> Of the 1,822 publications retrieved, 35 (32 studies) were included. Nearly all patients (98%, 1,992/2,024; 31 studies) were treated with surgery, and more studies used adjuvant radiotherapy than chemotherapy (24 *vs* 17 studies). Survival outcomes and recurrence rates varied among the studies because of the different histotypes, sites, and disease stages assessed. Only 5 studies reported safety findings. <u>Conclusions:</u> These findings highlight the lack of specific data available about soft-tissue sarcomas in the Asia-Pacific region. Better efforts to understand how the sarcoma is managed and treated will help improve patient outcomes in the region.**

Keywords: Asia-Pacific - incidence - sarcoma - soft-tissue neoplasms - survival

Introduction

Soft-tissue sarcomas (STS) are a heterogeneous group of rare tumours. More than 50 STS histotypes have been identified, with most having unique clinical, prognostic, and therapeutic features. Although less than 1% of all adult malignant tumours are STS (Fletcher et al., 2002a), their treatment and management is complex because many tumour-related (eg, histotype, site, size, depth, grade, primary *vs* recurrent) (Singer et al., 1994; 2000; Pisters et al., 1996) and treatment-related (eg, surgical margins, use of adjuvant therapy) (Singer et al., 2000) factors influence patient outcomes. Because these factors are inherently variable and because STS is rare, the management of patients with STS is best undertaken by an experienced multidisciplinary team in specialist centres to minimise recurrence, maximise survival, and preserve functionality and quality of life (Ray-Coquard et al., 2004; Luis et al., 2010; National Comprehensive Cancer Network, 2012).

The standard primary treatment for STS is surgical resection, with appropriate negative margins where possible (Clark et al., 2005; National Comprehensive Cancer Network, 2012). Surgery may be followed by adjuvant radiotherapy and/or chemotherapy, where indicated (Clark et al., 2005; National Comprehensive Cancer Network, 2012); however, the use of adjuvant chemotherapy is controversial and may not benefit patients with localised resectable sarcoma (Woll et al., 2012). Recent advances in using these treatments have led to better outcomes for most patients with STS (Gronchi et al., 2011; Colombo et al., 2012), particularly those with low-grade sarcomas (Singer et al., 2000; Clark et al., 2005). Throughout the Asia-Pacific region, however, survival outcomes for patients with cancer, including STS, differ (Sankaranarayanan and Swaminathan, 2011), partly because cultural, economic, social, and geographic differences among and within countries have resulted in diverse healthcare systems (Chongsuvivatwong et al., 2011). Also, in some Asia-Pacific countries, patients with STS often present with advanced disease (Wang and

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Tan, 2010) or may seek further management elsewhere after inadequate resection (Wong et al., 2004), both of which reduce the patient's chances of survival. However, because comprehensive studies of STS in this region are lacking, our knowledge of current management strategies is limited.

To better understand the treatment, management, and survival outcomes of patients with STS in the Asia-Pacific region, we performed a systematic review of the current literature. Currently across this region, efforts to formally collaborate in STS research and management are underway and this review was seen as an important exercise to better define areas of need. Specifically, this review examined the common histotypes, treatment patterns, and survival and safety outcomes reported in studies of adult patients with STS from a representative sample of Asia-Pacific countries. These countries (Australia, Hong Kong, Indonesia, Korea, Malaysia, New Zealand, Philippines, Singapore, Taiwan, and Thailand) reflect the cultural, economic, social, and geographic differences that exist within the Asia-Pacific region.

Materials and Methods

Database search strategy

MEDLINE via PubMed was searched on October 20, 2011, using the search strategy: (((#1 OR #2) AND #3) NOT #4) OR (((#1 OR #2) AND #3) OR #5), where the numbers represent the following search terms: 1) sarcoma OR sarcomas; 2) (neoplasm OR neoplasms OR tumor OR tumour OR tumors OR tumours OR cancer OR cancers) AND "soft tissue"; 3) Australia OR "Hong Kong" OR Indonesia OR Korea OR Malaysia OR "New Zealand" OR Philippines OR Singapore OR Taiwan OR Thailand; 4) bone neoplasm; and 5) extraskeletal OR "extra skeletal" OR extra-skeletal OR extraosseous OR "extra osseous" OR extra-osseous OR chondroosseous OR "chondro osseous" OR chondro-osseous. This search strategy was used to retrieve publications describing STS, including extra-skeletal, extra-osseous, and chondro-osseous STS not located in the bones or the joints, and to exclude publications of bone tumours. The search was restricted to publications from October 20, 2001, to October 20, 2011, and to publications of human patients. There were no restrictions on publication language.
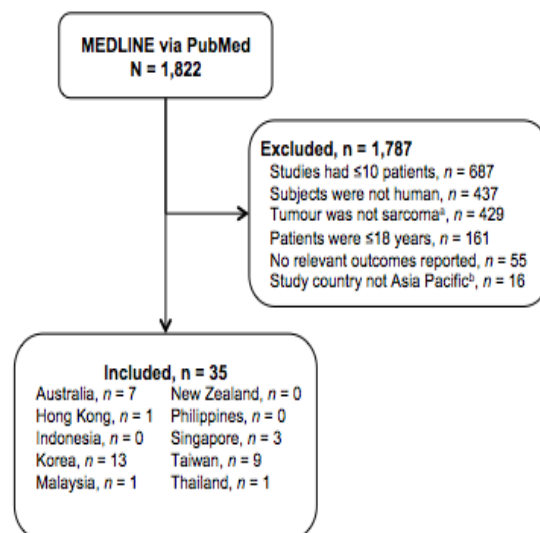
Publication selection

The abstracts of the retrieved publications were screened for possible full text review using prespecified inclusion and exclusion criteria. These criteria were also applied during the full text review of selected publications. Publications (systematic reviews, randomised or nonrandomised controlled trials, uncontrolled trials, or observational studies) of human (male or female) patients with STS that reported tumour characteristics, treatment patterns, efficacy outcomes, or safety outcomes were selected for review. Publications were excluded if subjects were nonhuman; all patients were younger than 18 years; the study had 10 or fewer patients, was done in countries other than Australia, Hong Kong, Indonesia, Korea, Malaysia, New Zealand, Philippines, Singapore,

Taiwan, and Thailand, or was a multicountry study of non-Asian and Asia-Pacific countries that did not include a subanalysis of data from the Asia-Pacific country; the STS was located in the bones or joints, was gastrointestinal stromal tumour or Kaposi's sarcoma, or the proportion of patients with benign soft-tissue tumours was greater than 20%; or no relevant tumour attributes or efficacy or safety outcomes were reported. Publications were included if the study involved patients younger than 18 years but the mean or median age was 18 years or older. The bibliographies of relevant reviews were searched for any additional articles that should be assessed.

Data extraction

A spreadsheet was developed for data collection and refined as data were extracted. Data were extracted by a researcher (Julie Monk, ProScribe Medical Communications) and reviewed by all authors. Data collected from each publication included publication and study information (study design, publication type, study period, follow-up duration, and study country), patient information (number, age, sex, ethnicity, and comorbidities), STS characteristics (histotype, site, grade, and stage), treatment patterns (surgery, radiotherapy, chemotherapy, and combinations thereof), efficacy and effectiveness outcomes [complete, partial, or stable response; progressive disease; death; local recurrence; disease-free, relapse-free, progression-free, or overall survival (OS)], and safety and tolerability outcomes (complications arising from surgery; adverse events; drug-related adverse events). As per the current World Health Organization guidelines for STS classification (Fletcher

Figure 1. Flow Diagram of Literature Search Results.
The search was restricted to studies of human patients with soft-tissue sarcoma that were published from October 20, 2001, to October 20, 2011. There were no restrictions on publication language. [a]Studies of sarcomas located in the bones or joints, gastrointestinal stromal tumour, or Kaposi's sarcoma, and studies where the proportion of patients with benign soft-tissue tumours was greater than 20% were excluded from review; [b]Studies from the following Asia-Pacific countries included in this review were Australia, Hong Kong, Indonesia, Korea, Malaysia, New Zealand, Philippines, Singapore, Taiwan, and Thailand

et al., 2002b), pleomorphic sarcoma has been used throughout this review to describe sarcomas classified as malignant fibrous histiocytoma. Not all data collected from the publications are reported in this review. Publications were sorted and analysed according to whether patients had primary or recurrent disease, and local or metastatic disease, because of the different treatment strategies required and different survival outcomes for these stages of disease. Percentages were calculated, when possible, if they were not provided in the original publication.

Results

Literature search results

A total of 1,822 abstracts were retrieved from MEDLINE and screened for inclusion (Figure 1). Overall, 1,787 publications were excluded, mostly because they were of studies of 10 or fewer patients (n=687), nonhuman subjects (n=437), or diseases other than STS (n=429). The remaining 35 publications (all English language) were included for analysis. Most publications (83%, 29/35) were from Australia, Korea, and Taiwan, with none from Indonesia, New Zealand, or Philippines. As 4 publications (Huang et al., 2006; 2008; 2010; Lin et al., 2006) reported data from one group of patients over time, only data from the most recent publication (Huang et al., 2010) were reviewed. Thus, we examined the findings of 32 studies.

Study and patient characteristics

The 32 studies were 1 prospective (Koh et al., 2009) and 31 retrospective observational studies. The study periods spanned the 1990s and/or 2000s, and dated back to the 1980s for 9 studies (Hsieh et al., 2003; Campbell et al., 2004; Hsu et al., 2004; Dickinson et al., 2006; Wu et al., 2006; Kim et al., 2007; 2008c; Huang et al., 2010; Han et al., 2011) and the 1970s for 1 study (Wang et al., 2009) (Table 1). The number of patients [minimum, 12 (Jun et al., 2010); maximum, 324 (Dickinson et al., 2006) was fewer than 50 in 17 of the 32 studies. Only 13 studies specified whether STS was primary or recurrent [8 primary (Dickinson et al., 2006; Hui et al., 2006; Wu et al., 2006; An et al., 2007; Kim et al., 2008a; Ng and Tan, 2009; Wang et al., 2009; Liu et al., 2010); 5 primary or recurrent (Hsieh et al., 2003; Kiatisevi et al., 2006; Moncrieff et al., 2008; Miki et al., 2010; Cho et al., 2011)]. Patients had local disease in 15 studies (Choong et al., 2003; Campbell et al., 2004; Hsu et al., 2004; Dickinson et al., 2006; Hui et al., 2006; An et al., 2007; Kim et al., 2007; 2008c; 2009; 2010; Pervaiz et al., 2008; Rudiger et al., 2009; Wang et al., 2009; Liu et al., 2010; Cho et al., 2011; Han et al., 2011), and local or metastatic disease in 7 studies (Wu et al., 2006; Chan et al., 2008; Moncrieff et al., 2008; Koh et al., 2009; Jun et al., 2010; Park et al., 2010; Lee et al., 2011). The remaining 10 studies did not specify whether disease was local or metastatic. Overall, pleomorphic

Table 1. Observational Studies of Soft-tissue Sarcoma: Study and Patient Characteristics

Publication		Study Period	N	Recurrent, n (%)	Metastatic, n (%)	Age, years (min, max)	% Male
Australia	Choong et al., 2003	1996-2001	54	NS	0 (0)	Median: 32 (17, 84)	56
	Campbell et al., 2004	1988-2001	25	NS	Excluded	Median: 40 (14, 70)	44
	Dickinson et al., 2006	1987-2002	324	45 (14), excluded from survival analysis		Median: 56 (3, 89)	52
	Hui et al., 2006	Jan 1996-Dec 2000	67	Excluded	Excluded	Median: 52 (17, 82)	61
	Moncrieff et al., 2008	1994-2007	21	7 (33)	3 (14)	Median: 60 (18, 85)	67
	Rudiger et al., 2009	1995-2005	25	NS	0 (0)	Mean: 56 (20, 83)	44
	Miki et al., 2010	Jan 1996-Dec 2005	91	7 (8)	NS	NR (15, 88)	58
Hong Kong	Wong et al., 2004	Jan 1995-May 2001	18	NS	NS	Mean: 55 (17, 80)	56
Korea	An et al., 2007	Feb 1996-Dec 2005	49	Excluded	Excluded	Mean: 54 (16, 78)	61
	Kim et al., 2007	1988-2002	47	NS	Excluded	Median: 61 (21, 79)	55
	Kim et al., 2008a	Feb 1996-Jun 2007	24	0 (0)	NS	NR (NR)	NR
	Kim et al., 2008b	Sep 1994-Mar 2007	22	NS	NS	Median: 43 (19, 58)	0
	Kim et al., 2008c	1980-2003	150	NS	Excluded	Median: 43 (11, 81)	60
	Kim et al., 2009	Jan 1995-May 2008	94	NS	0 (0)	Median: 56 (20, 80)	56
	Koh et al., 2009a	Jan 1997-Mar 2008	41	NS	15 (37)	Median: 37 (8, 81)	49
	Hong et al., 2010	Mar 1998-Mar 2009	15	NS	NS	Mean: 56 (36, 74)	73
	Jun et al., 2010	1995-2008	12	NS	6 (50)	Median: 26 (12, 57)	17
	Kim et al., 2010	Nov 2004-Dec 2008	55	NS	Excluded	Mean: 55 (29, 85)	0
	Park et al., 2010	Jul 1997-Dec 2008	18	NS	4 (22)	Mean: 45 (15, 79)	56
	Cho et al., 2011	Sep 1990-Jan 2010	99	20 (20)	Excluded	Median: 55 (26, 82)	56
	Han et al., 2011	Sep 1985-Sep 2007	104	NS	Excluded	Mean: 44 (5, 81)	59
Malaysia	Chan et al., 2008	Jan 1990-Dec 2005	36	NS	NR (47)	Mean: 52 (NR)b	56b
Singapore	Ng and Tan, 2009	1997-2007	27	Excluded	NS	Mean: 51 (27, 90)c	59c
	Wang and Tan, 2010	Jan 1999-Jan 2009	67	NS	NS	Mean: 52 (22, 84)	60
	Lee et al., 2011	Jun 1990-Jun 2005	21	NS	NR (3)	Mean: 52 (29, 71)	57
Taiwan	Hsieh et al., 2003	Jan 1987-Jan 1997	21	Included, NR (NR)	NS	Mean: 44 (22, 65)	0
	Hsu et al., 2004	Nov 1987-Dec 2000	76	NS	Excluded	Median: 52 (18, 83)	53
	Wu et al., 2006	Jan 1984-Jan 2003	51	Excluded	2 (4)	Median: 47 (26, 85)	0
	Wang et al., 2009	1974-2004	25e	0 (0)	0 (0)	Median: 49 (11, 70)	52
	Huang et al., 2010f	1986-2006	78	NS	NS	Median: 61 (16, 84)	56
	Liu et al., 2010	Jan 1997-Jan 2007	181	Excluded	Excluded	Median: 54 (5, 91)	58
Thailand	Kiatisevi et al., 2006	Jan 1992-Dec 2002	104	26 (25)	NS	Mean: 45 (10, 85)	46

*Abbreviations: max, maximum; min, minimum; NR, not reported; NS, not specified; aThis study was prospective. All other studies included in this systematic review were retrospective; bAge and % male calculated for 54 patients; only 36 patients had complete records for outcome analysis; cAge and % male calculated for 32 patients. Five patients were excluded from analyses because 2 had recurrent tumours, 2 refused further treatment, and 1 sought treatment overseas; dMedian is for 25 patients. The other patient was 68 years; eOf the 25 tumours, 8 were primary tumours and 17 were post-irradiated pleomorphic sarcoma; fBecause 4 publications (Huang et al., 2006; Lin et al., 2006; Huang et al., 2008; Huang et al., 2010) report data from a single group of patients over time, only data from the most recent publication (Huang et al., 2010) were reviewed

Table 2. Studies Reporting Findings from Patients with Primary Soft-tissue Sarcoma

Publication	Sarcoma Characteristics, n (%)				Treatment, n (%)	Follow-up, months (min, max)	Survival	Other Outcomes, n (%)
	Histotype	Site	Stage	Grade				
Local disease								
Dickinson et al., 2006	Pleomorphic sarcoma: 89 (27) Malignant liposarcoma: 76 (23) Synovial sarcoma: 46 (14) Leiomyosarcoma: 43 (13) Myxofibrosarcoma: 27 (8) Other: 53 (16)	NR	NR	NR	Surgery: 324 (100)	Median: 40 (2, 187)a	OS mean: 124 (95%CI 113-135) months	D: 87 (31) LR: 27 (10) DM: 27 (10)
Hui et al., 2006	Pleomorphic sarcoma: 25 (37) Liposarcoma: 15 (22) Synovial sarcoma: 8 (12) Leiomyosarcoma: 5 (7) Fibrosarcoma: 2 (3) Neurogenic sarcoma: 2 (3) Extraskeletal chondrosarcoma: 2 (3) Other: 8 (12)	Lower ext.: 53 (79) Upper ext.: 9 (13) Trunk: 5 (7)	NR	NS Low: 19 (28) High: 46 (69) NA: 2 (3)	preop EBRT: 67 (100) +Surgery: 66 (99)b Amputation: 1 (1) +po CT: 3 (5)c	Median: 49 (7, 83)	OS actuarial 5-year: 73% (95%CI 62%-84%)	D: 20 (30)d LR: 4 (6) DM: 18 (27) LR+DM: 1 (2)
An et al., 2007	Liposarcoma: 25 (51) Leiomyosarcoma: 9 (18) Pleomorphic sarcoma: 2 (4) Malignant PNST: 3 (6) Paraganglioma: 5 (10) Primitive neuroectodermal tumour: 1 (2) Carcinoid tumour: 1 (2) Myxoid spindle cell tumour: 2 (4) Ewing sarcoma 1 (2)	Retroperitoneum: 49 (100)	NR	NS 1: 14 (29) 2/3: 12 (24) Undetermined: 22 (45) NA: 1 (2)	Surgery: 42 (86) NS: 7 (14)	Mean: 27 (2, 102)	OS 5-year: 55%	D: 13 (27) LR: 7 (14) DM: 5 (10) LR+DM: 1 (2)
Wang and Tan, 2009	Pleomorphic sarcoma: 25 (100)e	Sinonasal: 25 (100)	AJCC T1: 9 (36) T2: 16 (64)	NS High: 25 (100)	Surgery: 23 (92) +po RT: 9 (36) Pallative: 2 (7)	Median: 18 (1, 216)	OS 5-year: 25%	D: 18 (72) LR: 11 (44) DM: 1 (4) LR+DM:1 (4)
Liu et al., 2010	Pleomorphic sarcoma: 50 (28) Liposarcoma: 50 (28) Synovial sarcoma 21 (12) Leiomyosarcoma: 17 (9) Malignant PNST: 10 (6) Fibrosarcoma: 6 (3) Other: 27 (15)	Lower ext.: 168 (93) Upper ext.: 13 (7)	NR	FNCLCC I: 41 (23) II: 65 (36) III: 75 (41)	Surgery: 181 (100) Amputation: 4 (2) +preop RT: 2 (1) +preop CT: 25 (14) +po RT: 67 (37) +po CT: 73 (40)f	Median: 43 (NR)	DSS actuarial 5-year: 71% (95%CI 63%-79%)	D: NR (NR) LR or DM: 83 (46)
Local and metastatic disease								
Wu et al., 2006	Leiomyosarcoma: 51 (100)	Uterus: 51 (100)	FIGO I: 41 (80) III: 7 (14) IV: 3 (6)	NS I: 23 (49) II: 8 (17) III: 16 (34)	Surgery: 51 (100) +po RT: 3 (6) +po CT: 16 (31)g	Median: 47 (2, 166)	OS 5-year: 67%	D: NR (NR) LR: 5 (10) DM: 7 (14) LR+DM: 4 (8) Unknown: 1 (2)
Local and metastatic disease not specified								
Kim et al., 2008	Intermediate liposarcoma: 10 (42) Malignant liposarcoma: 14 (58)	Retroperitoneum: 24 (100)	NR	NR	Surgery: 24 (100)	Median: 16 (4, 58)	NR	D: NR (NR) LR: 11 (46) DM: NR (NR)
Ng and Tan, 2009	Intermediate liposarcoma: 14 (52) Malignant liposarcoma: 13 (48)	Upper ext.: 5 (19) Lower ext.: 22 (81)	MTS IIA: 1 (4) IB: 15 (56) IIB: 11 (41)	NS Low: 17 (63) Int.: 7 (26) High: 3 (11)	Surgery 27: (100) +po RT: 14 (52) +po CT: 3 (11)h	Mean: 53 (2, 135)	OS 53-month: 93%	D: 2 (7) LR or DM: NR (15)

*Abbreviations: AJCC, American Joint Committee on Cancer for STS staging system, 6th edn; CI, confidence interval; CT, chemotherapy; D, dead; DM, distant metastases; DSS, disease-specific survival; EBRT, external beam radiotherapy; ext., extremities; FIGO, International Federation of Gynecology and Obstetrics for endometrial carcinoma, Vol 19; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer (National Federation of French Cancer Centres) grading system; LR, local recurrence; max, maximum; min, minimum; MTS, Musculoskeletal Tumour Society staging system; NA, not assessed; NR, not reported; NS, not specified; OS, overall survival; PNST, peripheral nerve sheath tumour; po, postoperative; preop, preoperative; RT, radiotherapy; aData are for 279 patients. Patients were excluded from survival analyses if they had presented with local recurrence or distant metastases; bOne patient did not proceed to surgery because distant metastases were detected after restaging; cChemotherapy was adriamycin-based chemotherapy; dOf the 20 patients, 15 died of causes related to soft-tissue sarcoma and 5 died of other causes; ePleomorphic sarcoma was either primary disease (n=8) or post-irradiated disease (n=17); fChemotherapy was anthracycline-based chemotherapy; gChemotherapy was cisplatin plus ifosfamide (n=4), cisplatin plus adriamycin allternating with cisplatin plus ifosfamide (n=3), cisplatin plus adriamycin plus cyclophosphamide (n=2), cisplatin plus adriamycin/epirubicin (n=2), and vincristine plus adriamycin plus cyclophosphamide (n=1); hChemotherapy agents not specified

Table 3. Studies Reporting Findings from Patients with Primary and Recurrent Soft-tissue Sarcoma

Publication	Sarcoma Characteristics, n (%)		Stage	Grade	Treatment, n (%)	Follow-up, months (min, max)	Survival	Other Outcomes, n (%)
	Histotype	Site						
Local disease								
Cho et al., 2011	Liposarcoma/leiomyosarcoma: NR (83)	Retroperitoneum: 99 (100)	NR	FNCLCC 1: NR (NR) 2/3: NR (81)	Surgery: 99 (100)	Median: 36 (1, 221)	DSS actuarial 5-year: 75%	D: 27 (27)a LR: 69 (70) DM: NR (NR)
Local and metastatic disease								
Moncrieff et al., 2008	Pleomorphic sarcoma: 10 (48) Angiosarcoma: 4 (19) Fibrosarcoma: 2 (10) Other: 5 (24)	Lower ext.: 18 (86) Upper ext.: 3 (14)	AICC I: 0 (0) II: 9 (43) III: 9 (43) IV: 3 (14)	NS High: 20 (95) NR, 1 (5)	ILI: 7 (33)b Neoadjuvant ILI: 14 (67)b +Surgery: 14 (67) +po RT: 10 (48)	Median: 28 (2, 91)	DSS: 62%	D: NR (NR) LR: 9 (43) DM: NR (NR)
Local and metastatic disease not specified								
Hsieh et al., 2003	Leiomyosarcoma: 21 (100)	Uterus: 21 (100)	FIGO I: 14 (67) II: 1 (5) III: 5 (24) IV: 1 (5)	NS I: 7 (33) 2: 10 (48)c 3: 4 (19)	Surgery: 21 (100) +po RT: 3 (14)c +po CT: 7 (33)d	Mean: 30 (4, 129)	OS 5-year: 58%	D: 8 (41) LR: 6 (29) DM: 3 (14)
Kiatisevi et al., 2006	Pleomorphic sarcoma: 21 (20) Liposarcoma: 21 (20) Synovial sarcoma: 13 (13) Fibrosarcoma: 8 (8) Leiomyosarcoma: 8 (8) Malignant PNST: 5 (5) Malignant hemangiopericytoma: 5 (5) Rhabdomyosarcoma 3 (3) Other 20 (19)	Lower ext.: 74 (71) Upper ext.: 19 (18) Head, neck & trunk: 11 (11)	NR	NS Low: 26 (25) High: 78 (75)	Surgery: 100 (96) +po RT: 51 (49) +po CT: 23 (22)e Palliative: 4 (4)	Median: 25 (1, 135)	DSS actuarial 3-year: 74%	D: 24 (23)f LR: 26 (25) DM: 29 (28)
Miki et al., 2010	Pleomorphic sarcoma: 46 (51) Liposarcoma: 21 (23) Malignant tumours of uncertain differentiation: 9 (10) Neurosarcoma: 8 (9) Leiomyosarcoma: 6 (7) Rhabdomyosarcoma: 1 (1)	Lower ext.: 53 (58) Upper ext.: 13 (14) Trunk: 13 (14) Pelvis: 9 (10) Retroperitoneum: 3 (3)	NR	NS I: 17 (19) II: 35 (38) III: 39 (43)	Preop RT: 91 (100) +Surgery: 91 (100) Amputation: 5 (5)	NR (1, 128)	NR	D: NR (NR) LR: 8 (9) DM: 27 (30)

*Abbreviations: AICC, American Joint Committee on Cancer for STS staging system, 6th edn; CT, chemotherapy; D, dead; DM, distant metastases; DSS, disease-specific survival; ext., extremities; FIGO, International Federation of Gynecology and Obstetrics for endometrial carcinoma, Vol 19; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer (National Federation of French Cancer Centres) grading system; ILI, isolated limb infusion; LR, local recurrence; max, maximum; min, minimum; NR, not reported; NS, not specified; OS, overall survival; PNST, peripheral nerve sheath tumour; po, postoperative; preop, preoperative; RT, radiotherapy; aOf the 27 patients, 25 died of causes related to soft-tissue sarcoma and 2 died of other causes; bCytotoxic drugs used for ILI were melphalan 5-10 mg/L of tissue and actinomycin D 50-100 μg/L of tissue. From 1994 to 1996, 1 patient had melphalan and actinomycin D; 3 patients had mitomycin C at 5-20 mg in addition to melphalan, and 1 patient had mitomycin (10 mg), doxorubicin (25 mg), and cisplatin (50 mg). Seven patients had ILI only for either an inoperable recurrence or for palliation; cOf the 3 patients who had pelvic radiotherapy, 1 patient had an intravaginal boost using Ir-192 source; dPatients had combination chemotherapy consisting of dacarbazine, doxorubicin, cyclophosphamide and/or etoposide; eChemotherapy agent not specified; fOf the 24 patients, 21 died of causes related to soft-tissue sarcoma and 3 died of other causes

sarcoma and liposarcoma were the most common histotypes reported (23 of 32 studies). Most patients were middle-aged or elderly; the mean or median age (reported in 30 studies) was 40 years or older in 27 studies. However, the minimum age (reported in 30 studies) was younger than 18 years in 14 studies. The percentage of male patients per study ranged from 17% (Jun et al., 2010) to 73% (Hong et al., 2010), excluding 4 studies of female patients with uterine and endometrial sarcomas (Hsieh et al., 2003; Wu et al., 2006; Kim et al., 2008a; 2010).

Studies of primary soft-tissue sarcoma

In the 8 studies of primary STS, disease was local (5 studies), local and metastatic (1 study), or not specified (2 studies; Table 2). The predominant STS histotypes were pleomorphic sarcoma and liposarcoma (7 of 8 studies). Sarcoma site was specific (retroperitoneum, extremities, uterus, or sinonasal) in 7 studies and was not reported in 1 study.

Treatment included surgery only (3 studies), surgery and radiotherapy (1 study), and surgery, radiotherapy, and chemotherapy (4 studies). Nearly all patients were treated with surgery: 100% in 5 studies and 86%, 92%, and 99% in the other 3 studies (Table 2). The remaining patients were not treated with surgery because it was not indicated (Wang et al., 2009), the surgery was biopsy only (An et al., 2007), or distant metastases were detected during restaging studies (eg, magnetic resonance imaging of primary tumour site) done after preoperative radiotherapy (Hui et al., 2006). Only 5 patients from 2 studies had amputations (Table 2). In 1 study, complications arising from surgery (minor or major dehiscence, infection, delayed healing, haematoma/ seroma, flap necrosis, and wound edge necrosis) affected 27 (41%) patients (Hui et al., 2006). Few patients (14%, 1 study) had preoperative chemotherapy, whereas 1% (1 study) and 100% (1 study) of patients had preoperative

Table 4. Studies Reporting Findings from Patients with Soft-tissue Sarcoma (primary or recurrent not specified)

Publication	Sarcoma Characteristics, n (%)		Stage	Grade	Treatment, n (%)	Follow-up, months (min, max)	Survival	Other Outcomes, n (%)
	Histotype	Site						
Local disease								
Choong et al., 2003	Pleomorphic sarcoma: 20 (37) Liposarcoma: 11 (20) Leiomyosarcoma: 6 (11) Synovial sarcoma: 5 (9) Fibrosarcoma: 3 (6) Myxoid sarcoma: 2 (4) Other: 7 (13)	Lower ext.: 39 (72) Upper ext.: 7 (13) Gluteal region: 4 (7) Neck: 2 (4) Back: 2 (4)	NR	NS I: 8 (15) II: 11 (20) III: 9 (17) IV: 26 (48)	Preop RT: 54 (100) +Surgery: 54 (100)	NR (NR)	NR	NR (NR)
Campbell et al., 2004	Synovial sarcoma: 25 (100)	Lower ext.: 18 (72) Upper ext.: 6 (24) Trunk: 1 (4)	NR	NS (nuclear) High: 9 (36) NR: 16 (64)	Surgery: 25 (100) Amputation: 2 (8) +po RT: 22 (88) +po CT: 2 (8)[a]	NR (5, 140)	OS mean: 91 (95% CI 66-115) months	D: 9 (36) LR: 1 (4) DM: 11 (44)
Hsu et al., 2004	Pleomorphic sarcoma: 76 (100)	Lower ext.: 30 (40) Upper ext.: 12 (16) Head & neck: 11 (14) Trunk: 11 (14) Pelvis: 6 (8) Other: 6 (8)	AJCC 1: 27 (36) 2: 28 (37) 3: 21 (28)	NS Low: 27 (36) High: 49 (64)	Surgery: 76 (100) +po EBRT: 31 (41)	Median: 93 (27, 188)	OS 5-year: 74%	D: NR (NR) LR: 22 (29) DM: 4 (5) LR+DM: 6 (8)
Kim et al., 2007	Pleomorphic sarcoma: 47 (100)	Lower ext.: 24 (51) Upper ext.: 14 (30) Trunk: 9 (19)	AJCC II: 21 (45) III: 26 (55)	FNCLCC II: 35 (74) III: 12 (26)	Surgery: 47 (100) +po RT: 8 (17) +Neoadjuvant & po CT: 12 (26)[a]	Median: 50 (9, 218)	OS 5-year: 59% (95% CI 45-73)	D: 20 (43) LR: 22 (47) DM: 21 (45)
Kim et al., 2008	Pleomorphic sarcoma: 53 (35) Liposarcoma: 32 (21) Synovial sarcoma: 17 (11) Fibrosarcoma: 8 (5) Malignant PNST: 14 (9) Leiomyosarcoma: 8 (5) Other: 18 (12)	Lower ext.: 79 (53) Trunk: 39 (26) Upper ext.: 32 (21)	NR	FNCLCC Low (1/2): 63 (42) High (3): 87 (58)	Surgery: 150 (100) +preop CT: 5 (3)[a] +po RT: 21 (14) +po CT: 16 (11)[a]	Median: 48 (NR)	OS actuarial 5-year: 82%	D: 21 (14) LR: 21 (14) DM: 3 (2) LR+DM: 15 (10)
Kim et al., 2009	Intermediate liposarcoma: 50 (53) Malignant liposarcoma: 44 (47)	Retroperitoneum: 44 (47) Lower ext.: 24 (26) Trunk: 17 (18) Upper ext.: 9 (10)	NR	NS Low: 72 (77) High: 22 (23)	Surgery: 94 (100) +po EBRT: 31 (33)	Median: 48 (5,166)	OS 5-year: 78%	D: 22 (23) LR: 31 (33) DM: 4 (4)
Rudiger et al., 2009	Pleomorphic sarcoma: 9 (36) Liposarcoma: 8 (32) Leiomyosarcoma: 4 (16) Synovial sarcoma: 3 (12) Lymphoma: 1 (4)	Adductor compartment: 25 (100)	NR	NS Low: 5 (20) High: 20 (80)	Preop RT: 20 (80) +Surgery: 25 (100) Amputation: 1 (4) +po RT: 2 (8)	Mean: 42 (6, 119)[b]	OS 5-year: 72%	D: 5 (23) LR: NR (NR) DM: NR (NR)
Kim et al., 2010	Carcinosarcoma: 21 (38) Leiomyosarcoma: 20 (36) ESS: 14 (25)	Uterus: 55 (100)	FIGO I: 23 (42) II: 5 (9) III: 27 (49)	NS Low: 6 (11) ESS NR: 49 (89)	Surgery: 55 (100) +po RT: 26 (47) +po CT: 15 (27)[a]	Median: 26 (2, 63)	NR	NR (NR)
Han et al., 2011	Pleomorphic sarcoma: NR (35) Synovial sarcoma: NR (21) Liposarcoma: NR (13) Fibrosarcoma: NR (8) Leiomyosarcoma: NR (6)	Lower ext.: 62 (60) Upper ext.: 32 (31) Trunk: 10 (9)	NR	FNCLCC I: 6 (6) II: 54 (52) III: 44 (42)	Surgery: 104 (100) Amputation: 7 (6) +po RT: 44 (42) +po CT: 16 (15)[a]	Median: 56 (2, 200)	DSS actuarial 5-year: 88%	D: 16 (15)[c] LR: 25 (24) DM: NR (NR)
Local and metastatic disease								
Chan et al., 2008	Pleomorphic sarcoma: 36 (100)	Ext.: 30 (83) Trunk & thorax: 6 (17)	NR	NR	Surgery: 32 (89) Amputation: 11 (31) +po RT: 4 (11) +po CT: 13 (36)[d] Palliative: 4 (11)	NR	OS 5-year: 30%	D: NR (NR) LR or DM: NR (33)

Table 4 (continued). Studies Reporting Findings from Patients with Soft-tissue Sarcoma (primary or recurrent not specified)

Publication	Histotype	Sarcoma Characteristics, n (%) Site	Stage	Grade	Treatment, n (%)	Follow-up, months (min, max)	Survival	Other Outcomes, n (%)
Koh et al., 2009	Synovial sarcoma: Monophasic: 22 (54) Biphasic: 19 (46)	Ext.: 27 (66) Trunk: 14 (34)	NR	NR	Surgery 41: (100) +po EBRT: 24 (59) +po CT: 21 (51)[a]	Median: 32 (4, 216)	NR	D: 15 (37) LR: 7 (17) DM: 7 (17)
Jun et al., 2010	Alveolar soft part sarcoma: 12 (100)	Lower ext.: 6 (50) Uterus: 2 (17) Trunk: 1 (8) Neck: 1 (8) Unknown: 2 (17)	TNM TxNxM1: 2 (17) T1N0M0: 5 (42) T1N0M1: 3 (25) T2N0M0: 1 (8) T2N0M1: 1 (8)	NR	CT: 4 (33)[e] Surgery: 7 (58) +po RT: 1 (8) +po CT: 3 (25)[f] Lost-to-follow-up: 1 (8)	Up to 94 (NR)[g]	OS median: 53.2 (95% CI 41-66) months	D: 7 (58) LR: 0 (0) DM: 3 (25) LR+DM: 1 (8)
Park et al., 2010	Uncertain differentiation: 11 (61) Pleomorphic sarcoma: 3 (17) Myxofibrosarcoma: 2 (11) Leiomyosarcoma: 2 (11)	Lower ext.: 13 (72) Upper ext.: 4 (22) Popliteal area: 1 (6)	NR	WHO III: 18 (100)	NR	NR (NR)	NR	D: NR (NR)
Lee et al., 2011	Intermediate liposarcoma: 13 (62) Malignant liposarcoma: 8 (38)	Retroperitoneum: 21 (100)	NR	FNCLCC 1: 11 (52) 2: 3 (14) 3: 7 (33)	Surgery: 21 (100)	Median: 62 (1, 125)	OS 5-year: 49%	D: NR (NR) LR or DM: 11 (52)
Local and metastatic disease not specified								
Wong et al., 2004	Liposarcoma: 5 (28) Dermatofibrosarcoma protuberans: 5 (28) Pleomorphic sarcoma: 4 (22) Leiomyosarcoma: 1 (6) Myxofibrosarcoma: 1 (6) Undifferentiated sarcoma: 2 (11)	Upper ext.: 9 (50) Lower ext.: 5 (28) Trunk: 4 (22)	NR	NR	Surgery: 16 (89) +po EBRT: 3 (17) +po EBRT and BT: 9 (50) EBRT: 2 (11)	Mean: 42 (23, 100)	NR	D: 1 (6)[h] LR: 0 (0) DM: 2 (11)
Kim et al., 2008	ESS: 22 (100)	Endometrium: 22 (100)	NR	NS Low: 22 (100)	Surgery: 22 (100) +po RT: 2 (9) +po CT: 4 (18)[i]	Median: 77 (12, 202)	OS 10-year: 82%	D: 3 (14) LR or DM: 10 (46)
Hong et al., 2010	Dedifferentiated liposarcoma: 15 (100)	Retroperitoneum: 15 (100)	NR	NR	Surgery: 15 (100)	NR	NR	D: NR (NR) LR: 5 (33) DM: NR (NR)
Huang et al., 2010	Myxofibrosarcoma: 78 (100)	Ext.: 57 (73) Axial: 21 (27)	AJCC I: 14 (18) II: 30 (38) III: 30 (38) ND: 4 (5)	FNCLCC 1: 31 (40) 2: 36 (46) 3: 11 (14)	Surgery: 78 (100) +po RT: 23 (30) +po CT: 10 (13)[a]	Median: 54 (2, 201)[k]	DSS 5-year: 67%	D: 20 (27)[l] LR: NR (NR) DM: NR (NR)
Wang et al., 2010	Adipocytic: 25 (37) Uncertain differentiation: 25 (37)[f] Myofibroblastic: 8 (12) Smooth muscle: 4 (6) Skeletal muscle: 2 (3) Chondro-osseous: 2 (3) Vascular: 1 (2)	Lower ext.: 59 (88) Upper ext.: 8 (12)	AJCC Ia: NR (7) Ib: NR (7) IIa: NR (26) IIb: NR (12) IIc: NR (3) III: NR (43) IV: NR (3)	NS High: NR (61) NR: NR (39)	Surgery: 67 (100) *Amputation: NR (6)*	Mean: 46 (1, 112)	NR	D: NR (24) LR: NR (21) DM: NR (33)

*Abbreviations: AJCC, American Joint Committee on Cancer for STS staging system, 6th edn; BT, brachytherapy; CI, confidence interval; CT, chemotherapy; D, dead; DM, distant metastases; DSS, disease-specific survival; EBRT, external beam radiotherapy; ESS, endometrial stromal sarcoma; ext., extremities; FIGO, International Federation of Gynecology and Obstetrics for endometrial carcinoma, Vol 19; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer (National Federation of French Cancer Centres) grading system; LR, local recurrence; max, maximum; min, minimum; ND, not determined; NR, not reported; NS, not specified; OS, overall survival; PNST, peripheral nerve sheath tumour; po, postoperative; preop, preoperative; RT, radiotherapy; WHO, World Health Organization; [a]Chemotherapy agent not specified; [b]Follow-up data were available for 22 of the 25 patients; [c]Of the 16 patients, 14 died of causes related to soft-tissue sarcoma and 2 died of other causes; [d]Chemotherapy agents given were doxorubicin, ifosfamide, cisplatin and 3 patients had doxorubicin, ifosfamide, cisplatin and 3 patients had doxorubicin, ifosfamide, cisplatin or ifosfamide or a combination of vincristine, doxorubicin, cyclophosphamide, etoposide, and ifosfamide or doxorubicin, ifosfamide, and cisplatin; [e]One patient had etoposide, ifosfamide, cisplatin and 3 patients had doxorubicin, ifosfamide, cisplatin; [f]Chemotherapy agents were ifosfamide doxorubicin plus ifosfamide; etoposide, adriamycin, and cyclophosphamide; ifosafamide, adriamycin, and cyclophosphamide; or adriamycin and cisplatin; [g]Because 4 publications (Huang et al., 2006; Lin et al., 2006; Huang et al., 2008; Huang et al., 2010) report data from a single group of patients over time, only data from the most recent publication (Huang et al., 2010) were reviewed; [k]Follow-up data were available for 74 of the 78 patients; [l]Of the 20 patients, 15 died of causes related to soft-tissue sarcoma and 5 died of other causes

radiotherapy. A mixed proportion of patients had postoperative radiotherapy (6-52%; 4 studies) and postoperative chemotherapy (5-40%; 4 studies).

The mean/median follow-up time varied from 16 to 53 months (Table 2). Survival rates [OS or disease-specific survival (DSS); reported in 7 studies] differed and were lowest (25%; 5-year OS rate) for sinonasal pleomorphic sarcoma (100% high grade) (Wang et al., 2009) and highest (93%; 53-month OS rate) for extremity liposarcoma (11% high grade) (Ng and Tan, 2009). The rate of local recurrence and/or distant metastases varied from 15% to 52% (Table 2). Local recurrence and/or distant metastases was reported for about 50% of patients with sinonasal pleomorphic sarcoma (100% high grade) (Wang et al., 2009), extremity sarcoma [41% Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grade III] (Liu et al., 2010), and retroperitoneal liposarcoma (grade not reported) (Kim et al., 2008a). Adverse events were reported in only 1 study (complications arising from surgery).

Studies of primary and recurrent soft-tissue sarcoma

In the 5 studies of primary and recurrent STS, disease was local (1 study), local or metastatic (1 study), or not specified (3 studies; Table 3). The predominant STS histotypes were pleomorphic sarcoma, liposarcoma, or leiomyosarcoma. Sarcoma site was specific in 3 studies (retroperitoneum, extremities, or uterus) and varied in 2 studies.

Treatment included surgery (1 study), surgery and radiotherapy (1 study), and surgery, radiotherapy and chemotherapy (3 studies; Table 3). Nearly all patients were treated with surgery: 100% in 3 studies, and 67% and 96% in the other 2 studies (Table 3). The remaining patients were not treated with surgery because it was not indicated (Kiatisevi et al., 2006; Moncrieff et al., 2008) or the tumour was an inoperable recurrence (Moncrieff et al., 2008). In 1 study, 5 patients (5%) had amputations (Miki et al., 2010). In another study, all patients had isolated limb infusion, 67% as preoperative chemotherapy and 33% as treatment for inoperable recurrence or palliation (Moncrieff et al., 2008). Complications arising from isolated limb infusion were reported; 3 (14%) patients developed grade IV toxicity (Moncrieff et al., 2008). Preoperative chemotherapy was not given in the other 4 studies (Table 3). In 1 study, 100% of patients had preoperative radiotherapy (Miki et al., 2010). A proportion of patients had postoperative radiotherapy (14-49%; 3 studies) and postoperative chemotherapy (22% and 33%; 2 studies; Table 3).

The mean/median follow-up time (reported in 4 studies) varied from 25 to 36 months (Table 3). Survival rates (OS or DSS; 4 studies) differed and were lowest (58%; 5-year OS) for extremity, head, neck, and trunk sarcoma (19% grade 3) (Hsieh et al., 2003) and highest (75%; actuarial 5-year DSS) for retroperitoneal sarcoma (81% FNCLCC grade 2/3) (Cho et al., 2011), despite the rate of local recurrence and/or distant metastases in this study being 70% (median follow-up time=15.9 months). In the 4 other studies, the rate of local recurrence and/or distant metastases varied and was as low as 39% in a study

of extremity, trunk, pelvic, and retroperitoneal sarcoma (43% grade III) (Miki et al., 2010). Adverse events were reported in only 1 study (complications arising from isolated limb infusion).

Studies of soft-tissue sarcoma: primary or recurrent status not specified

In the 19 studies that did not specify whether STS was primary or recurrent, disease was local (9 studies), local or metastatic (5 studies), or not specified (5 studies; Table 4). The predominant STS histotypes were pleomorphic sarcoma and liposarcoma (11 studies). Sarcoma site was specific in 6 studies (retroperitoneum, extremities, uterus, adductor compartment, or endometrium) or varied in 13 studies, in which the extremities were the predominant site (50-96%; 12 studies).

Local disease

In the 9 studies of patients with local disease, treatment included surgery and radiotherapy (4 studies), and surgery, radiotherapy, and chemotherapy (5 studies; Table 4). All patients were treated with surgery, among whom only 9 patients from 3 studies had amputations. In 1 study (Rudiger et al., 2009), major complications arising from surgery (infection, wound breakdown necessitating debridement and re-closure, giant haematoma, severe permanent lymphoedema, intra-operative catheterisation for femoral artery spasm) were reported for 7 (26%) patients (80% of all patients had received preoperative radiotherapy). Few patients (3%, 1 study) had preoperative chemotherapy, whereas most patients (80% and 100%) in 2 studies had preoperative radiotherapy (Table 4). A mixed proportion of patients had postoperative radiotherapy (8-88%; 8 studies). In 4 studies, 8% to 27% of patients had postoperative chemotherapy. Pre- and postoperative chemotherapy was given to 26% of patients in 1 study.

The mean/median follow-up time (reported in 7 studies) varied from 26 to 93 months (Table 4). Survival rates (OS or DSS; 7 studies) varied from 59% (5-year OS) for extremity and trunk pleomorphic sarcoma (26% FNCLCC grade III) (Kim et al., 2007) to 88% (actuarial 5-year DSS) for extremity and trunk sarcoma (42% FNCLCC grade III) (Han et al., 2011). The rate of local recurrence and/or distant metastases (5 studies) varied from 24% for extremity and trunk sarcoma (42% FNCLCC grade III) (Han et al., 2011) to 48% for extremity and trunk synovial sarcoma (36% high grade) (Campbell et al., 2004). In a study of extremity and trunk pleomorphic sarcoma (26% FNCLCC grade III) (Kim et al., 2007), the rates of local recurrence and distant metastases were 47% and 45%, respectively; however, whether patients had both local recurrence and distant metastases was not specified. Adverse events were reported in only 1 study (complications arising from surgery).

Local and metastatic disease

In the 5 studies of patients with local or metastatic disease, treatment included surgery (1 study) and surgery, radiotherapy, and chemotherapy (3 studies), and was not reported in 1 study (Table 4). Nearly all patients were treated with surgery: 100% in 2 studies and 58% and

89% in the other 2 studies. The remaining patients were not treated with surgery because it was not indicated (Chan et al., 2008; Jun et al., 2010). In 1 study, 11 (31%) patients had amputations (Chan et al., 2008). Postoperative morbidity was reported for 6 (29%) patients in 1 study of retroperitoneal liposarcoma (Lee et al., 2011). No patients had preoperative radiotherapy or chemotherapy. A mixed proportion of patients had postoperative radiotherapy (8-59%; 3 studies) or chemotherapy (25-51%; 3 studies). Four patients (1 study) had chemotherapy as palliative treatment for alveolar soft part sarcoma (Jun et al., 2010).

The follow-up time (reported in 3 studies) was 32 and 62 months (median) for 2 studies and up to 94 months for 1 study (Table 4). Overall survival (5-year rates; 2 studies) was lower for extremity and trunk pleomorphic sarcoma (30%; grade not reported) (Chan et al., 2008) than retroperitoneal liposarcoma (49%; 33% FNCLCC grade 3) (Lee et al., 2011). The rate of local recurrence and/or distant metastases (4 studies) varied from 33% for extremity and trunk pleomorphic sarcoma (grade not reported) (Chan et al., 2008) to 52% for retroperitoneal liposarcoma (33% FNCLCC grade 3) (Lee et al., 2011). Adverse events were reported in only 1 study (postoperative morbidity).

Local and metastatic disease status unknown

In the 5 studies of patients whose local or metastatic disease status was unknown, treatment included surgery (2 studies), surgery and radiotherapy (1 study), and surgery, radiotherapy, and chemotherapy (2 studies; Table 4). Nearly all patients were treated with surgery: 100% in 4 studies and 89% in the other study. The remaining patients were not treated with surgery because it was not indicated; however, they were treated with radiotherapy (Wong et al., 2004). In 1 study of extremity sarcomas (Wang and Tan, 2010), 6% of patients had amputations, and an overall wound infection rate of 9.8% was reported. No patients had preoperative radiotherapy or chemotherapy. A low proportion of patients had postoperative radiotherapy (9-30%; 3 studies) or chemotherapy (13% and 18%; 2 studies). In 1 study, 50% of patients had postoperative external beam radiotherapy and brachytherapy (Wong et al., 2004).

The mean/median follow-up time (reported in 4 studies) ranged from 42 to 77 months (Table 4). Overall survival (2 studies) was 67% (5-year rate) for extremity and axial myxofibrosarcoma (14% FNCLCC grade 3) (Huang et al., 2010) and 82% (10-year rate) for endometrial stromal sarcoma (0% high grade) (Kim et al., 2008b). The rate of local recurrence and/or distant metastases (4 studies) varied from 11% for extremity and trunk sarcoma (grade not reported) (Wong et al., 2004) to 54% for extremity sarcoma (61% high grade) (Wang and Tan, 2010). Adverse events were reported in only 1 study (wound infection).

Discussion

This is the first systematic review of publications reporting findings on patients with STS in the Asia-Pacific region. This review highlights the scarcity of published data about STS treatment, management, and survival outcomes in this region. The strength of evidence of the included studies was limited; most studies were from 3 of the 10 study countries, there were no prospective controlled studies, patient numbers were small, and study periods dated back to the 1980s. Patients with STS require tailored and multidisciplinary treatment and management; however, this approach, and the resources needed to study and publish treatment practices, may be lacking in parts of the Asia-Pacific region. Further, differences in healthcare systems throughout the region (Chongsuvivatwong et al., 2011) may have contributed to the variability in reported outcomes. Overall, these findings emphasise the need for a comprehensive assessment of STS treatment, management, and outcomes in the Asia Pacific and are a critical first step towards developing clinical and research collaborations in the region.

All but a few patients in the included studies were treated with surgery, either alone or with adjuvant radiotherapy and/or chemotherapy. This finding aligns with current guidelines for STS treatment (Casali et al., 2010; National Comprehensive Cancer Network, 2012). Adjuvant radiotherapy has been shown to improve local control but not survival (Pisters et al., 2007), and its use depends on several factors, such as tumour size and location, the preferences of the treating physician and institution, and the resection margins (eg, involved, close, or clear). Adjuvant radiotherapy was administered to some patients, either preoperatively (1-100%) or postoperatively (6-88%), in 24 of the included studies. Preoperative radiotherapy, which may allow for the use of smaller field sizes and lower radiation doses and have lower long-term morbidity than postoperative radiotherapy (Pisters et al., 2007), seemed to be the standard of care at an Australian study centre (Choong et al., 2003; Hui et al., 2006; Rudiger et al., 2009; Miki et al., 2010), despite the potential for acute postoperative wound complications (Hui et al., 2006; Rudiger et al., 2009). Although the use of adjuvant chemotherapy may help local control, its marginal, if any, survival benefit (Pervaiz et al., 2008; Woll et al., 2012) has generally restricted its use to treatment of metastatic disease (Casali et al., 2010; National Comprehensive Cancer Network, 2012). Adjuvant chemotherapy was administered to some patients, either preoperatively (3-67%) or postoperatively (5-40%), in 17 of the included studies. However, the treatment patterns described do not necessarily reflect current practice because the study periods for many studies date back to the late 1970s or 1980s. The standard of care for sarcoma has changed substantially since then, from radical resection and amputation to definitive surgery and the use of adjuvant radiotherapy, where indicated (Colombo et al., 2012). In contrast, the use of adjuvant chemotherapy has become less frequent, especially in recent years, with successive studies failing to demonstrate a significant survival advantage (Pervaiz et al., 2008; Woll et al., 2012).

Survival outcomes and recurrence, when reported, varied among the included studies, which may be attributed to several factors. One factor is the range of sarcoma histotypes, sites, grades, and stages of disease assessed, which all influence patient prognosis. In this

review, for example, the 5-year OS rate was about 50% for retroperitoneal liposarcoma (33% FNCLCC grade 3) (Lee et al., 2011), whereas the 53-month OS rate was 93% for extremity liposarcoma (11% high grade) (Ng and Tan, 2009). The quality of surgery also plays a key role in survival outcomes (Stojadinovic et al., 2002; Gronchi et al., 2005) and may have differed across, and possibly within, the centres of the included studies. In addition, access to radiotherapy or chemotherapy agents may have been limited in some of the study countries; however, most publications were from countries (Australia, Korea, and Taiwan) where access to these treatments is unlikely to be a major issue. Although survival outcomes in some studies may have been favourably skewed because they included patients with benign tumours, we limited this variable by excluding publications in which more than 20% of patients had benign tumours.

Pleomorphic sarcoma and liposarcoma were the predominant histotypes described in the included studies, and most sarcomas were located in the extremities. These findings are consistent with what has been reported worldwide (Fletcher et al., 2002a; Clark et al., 2005; Mankin and Hornicek, 2005). Interestingly, some of the sarcomas in the included studies were documented to have known or suspected causes, such as post-irradiated sinonasal pleomorphic sarcoma situated within the radiation field for previous nasopharyngeal carcinoma (Wang et al., 2009). However, most STS arise without an apparent cause (Fletcher et al., 2002a) and most included studies did not document causative factors.

Although we searched for studies from 10 representative Asia-Pacific countries, most of the studies included for review were from Australia, Korea, and Taiwan. As such, our findings may not be applicable to the entire Asia-Pacific region. A potential reason for this imbalance may include differences among countries in the availability of, or patient access to, specialist facilities that detect, diagnose, and treat STS (Sankaranarayanan and Swaminathan, 2011). Other demands on health resources, such as health tourism and the trade of health workers (Acuin et al., 2011), may influence the availability of these facilities. Also, patients in countries poorly resourced to treat STS may opt to go to another country, if possible, for treatment (Ng and Tan, 2009) or seek treatment from private providers. Another potential reason is that because sarcoma is rare, some countries may simply lack sufficient cases to publish meaningful findings on the outcomes of treating sarcoma. In addition, they may lack resources, infrastructure, and academically focused clinicians to conduct research and publish findings. Until such data become available, it is difficult to accurately comment on the quality of care delivered in those countries.

We acknowledge that there are several limitations with our study. First, as with any systematic review, relevant publications may have been inadvertently excluded despite a comprehensive literature search. Second, data from the included studies cannot be pooled for analysis because of the varied reporting of survival outcomes. In addition, the reported sarcoma grade and diagnosis may not be accurate because some studies reassessed pathology slides to confirm or reclassify diagnosis, whereas other studies simply reviewed patient records. Third, the strength of evidence was limited because all included studies had an observational study design with only 1 prospective study and because more than half of the studies had fewer than 50 patients even though studies with 10 or fewer patients were excluded. Last, few studies (5 of 32) reported safety outcomes and those that did mostly reported complications arising from surgery. With the increasing use of adjuvants, such as chemotherapy agents, for sarcoma treatment, monitoring and reporting safety outcomes is paramount.

Our review indicates that data about the treatment and management of patients with STS and their outcomes in the Asia-Pacific region are lacking. Among the included studies, survival outcomes and recurrence, when reported, differed and few reported safety outcomes. The treatment and management of STS requires a multidisciplinary approach; however, healthcare systems within and among Asia-Pacific countries are in various states of evolution (Chongsuvivatwong et al., 2011). This may have adverse consequences for patients by limiting the availability of, or access to, facilities that detect, diagnose, and treat STS. As such, we need to continually invest in collaborative efforts to better understand how STS affects patients within the Asia-Pacific region. By doing so, we will be able to better manage patients from diagnosis to follow-up and help improve survival outcomes and quality of life.

Acknowledgements

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