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Early Local Recurrence Presents Adverse Effect on Outcomes of Primary Breast Sarcoma

A Retrospective Study From Single Institute in China

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Abstract: Primary breast sarcomas (PBSs) are spectrum heterogeneous sarcomas in breast and the optimal treatment for them is still under discussion. Our study was to investigate clinical characteristics and identify potential prognostic factors for this rare malignancy.

The authors retrospectively reviewed 38 patients with PBSs between October 2000 and February 2014 in FuDan University Shanghai Cancer Center. Local control rate and overall survival (OS) were determined by Kaplan–Meier actuarial method. Univariate analysis and Cox proportional hazards model were applied to identify potential prognostic factors.

With median follow-up of 40.19 months, 14 patients (14/38) were found with local recurrence. Extensive operation like mastectomy was not superior to local resection ($P = 0.167$). Three-year recurrence-free survival and OS rate were 61.9% and 89%, respectively. Larger tumor size and local recurrence were indicated as unfavorable prognostic factors in univariate analysis. Cox model identified narrow interval of recurrence free survival as an unfavorable factor ($P = 0.048$).

Surgery remains crucial treatment for PBSs. Mastectomy, however, is not routinely necessary if clear margin could be achieved by local excision. Early recurrence indicates a poor OS.

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Abbreviations: LRC = locoregional control, OS = overall survival, PBSs = primary breast sarcomas.

INTRODUCTION

Primary breast sarcomas (PBSs) are rare mesenchymal-derived tumors, accounting for only 1% of breast tumors and less than 5% of sarcomas in all locations. Primary breast sarcomas are recognized as a heterogeneous group of tumors with different biologic properties, in which the pure sarcomas lacking of epithelial component are even rare as these comprise only 0.5% of the breast tumors.[1,2] Sarcomas that are composed principally of mesenchymal cells could be identified as benign, malignant, and tumor-like lesions, some of which occur predominantly in the breast. It's reported that the most common subtypes are malignant fibrohistiocytoma, (myxo)-fibrosarcoma, angiosarcoma, and spindle cell sarcoma. Several other subtypes, such as leiomyosarcoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma, osteosarcoma, just have been described as a small sample of case series or as case reports.[3]

The prevalence, etiologic factors, clinical and prognosis of PBSs are less known, compared with the epithelial breast cancers or those occurring in somatic soft tissues and skin. Owing to the low incidence and distinct histologic subtypes of the PBSs, it is hard to reach consensus regarding the treatment of this unusual disease. Current clinical management is mostly extrapolated from soft tissue sarcomas, requiring tailored and multidisciplinary treatments involved. Initial surgical resection is preferred to localized PBSs irrespective of the surgical procedure as far as the margin is clear.[4] Because metastatic pattern is believed to be less relevant to lymph node route, axillary lymph node dissection is not mandatory in the surgical procedure unless palpable lymph nodes are presented.[5]

Moreover, there is no explicit information available concerning the roles of radiotherapy or chemotherapy in PBSs. According to ESMO guideline for soft tissue and visceral sarcoma, radiotherapy is recommended in selected cases with high risk of recurrence.[6] Barrow[7] and Pancavel,[8] however found that administration of adjuvant radiotherapy in breast sarcoma failed to reach statistical significance. Majority of PBSs presented a relatively poor response to chemotherapy with doxorubicin and ifosfamide as the main agents.[9] Neoadjuvant chemotherapy might be advised in certain cases to improve probability of R0 resection, but its role in the treatment is still not clear.[10] Because neither prospective studies nor large sample investigation was available to consolidate the medical evidence of PBSs, the standard for definitive and optimal treatment strategy is variable between different doctors and medical institutions.

Therefore, the purpose of this study is to explore the PBSs characteristics and optimal treatment in Chinese population, as well as potential prognostic factors under the current clinical practice.

MATERIALS AND METHODS

Patients and Disease Criteria

A retrospective mesenchymal tumors database was searched for all patients with breast sarcoma presenting between

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October 2000 and February 2014 in Fudan University Shanghai Cancer Center. Review of data for this investigation was approved by the Institutional Review Board of Cancer Hospital, Fudan University. Total of 38 female patients histologically diagnosed as PBSs were involved in the current analysis, excluding cytosarcoma phyllodes tumors because of their epithelial pathologic feature concerning distinct histologic and biologic behavior.[11] Histologic diagnosis was confirmed in each case through review of the slides by experienced pathologists at our institute before treatment. The clinical and pathologic records of each patient were reviewed retrospectively with particular reference to clinical characteristics, tumor pathology, surgical approach and margin status, clinical stage, adjuvant treatment and outcomes. Tumors were defined according to the World Health Organization Classification of Tumours of Soft Tissue and Bone, fourth edition.[12] Following data was recorded and completed in August 2014.

Surgical resection was performed as the first modality of treatment in operable patients. Initial surgical procedure was defined as local resection, wide local resection, and mastectomy according to the surgical margin (>1 cm, ≥ 3 cm and surgical removal of a breast). Although treatment approaches to axilla might vary in different patients according to patients' preoperative evaluations and surgeons' experiences, axillary lymph nodes dissection was not routinely recommended in our cancer center for its low probability of metastasis in PBSs. Adjuvant treatment, including radiotherapy and/or chemotherapy was required as an individualized condition.

Statistical Analysis

The main endpoints of current study were local control and overall survival (OS) of patients with PBSs who underwent the surgical ablation. Time to local recurrence was defined as the time from surgery to radiologic diagnosis followed by pathologic confirmation of local recurrence. Time to metastasis was calculated from surgery to initial distant metastasis identified by imaging diagnosis with or without biopsy. The OS was defined as the time from the first treatment to either death or the last contact date, whichever happened first. The data of cases lost follow-up or observed alive till end-of-study were both calculated as censored values.

The Kaplan–Meier method was used to calculate survival curves, whereas curves' comparison was performed using the log-rank test. Univariate analysis was performed based on the following factors: age, menopausal status, tumor size, histological type and grade, surgical procedure, axillary dissection, and local recurrence. Multivariate analysis was performed to determine OS with adjustment for covariates, by using Cox regression model to test the following variables, including: tumor size, histologic type and grade, surgical procedure, time to local recurrence, and time to metastasis. All the statistical analyses were done by SPSS, version 11. Two-sided $P < 0.05$ was considered statistically significant.

RESULTS

From 2000 to 2014, a total of 38 female patients collected in this analysis were identified as PBSs. The median follow-up period of this study was 40.19 (range 6–165) months. None of patients had previous history of any other malignant tumor or irradiation to the ipsilateral breast. Only 1 patient had the breast augmentation surgery with breast implants. Twenty-eight patients (73.7%) were younger than 50 years with the median age at the first diagnosis being 35 years (16–70 years).

Pathology and Management

Primary breast sarcomas consisted of a group of different histologic subtypes. Mainly 8 categories were diagnosed in this study as follows: angiosarcoma, dermatofibrosarcoma protuberans, undifferentiated sarcoma, pleomorphic fibrosarcoma, liposarcoma, rhabdomyosarcoma, conventional osteosarcoma, and Ewing sarcoma. Angiosarcoma presented as the most common histologic type in this group. The histologic grade of each patient was assessed according to Rosen 3-tier system and French Federation of Cancer Centers Sarcoma Group for nonangiosarcoma: 10 (26.3%) as grade 1, 22 (57.9%) asgrade 2, and 6 (15.8%) as grade 3. The baseline characteristics and the treatment modalities of the patients were shown in Table 1.

In current series, 2 patients were diagnosed by excisional biopsy before transferring to our institute. Core needle biopsy in combination with imaging was considered as most frequent preoperative assessment in our institute and other 36 patients were diagnosed by core needle biopsy before operation. All the patients underwent surgery with curative intent, and among them, only 1 patient received neoadjuvant chemotherapy because of the large palpable mass over 10 cm in diameter. After 2 cycles preoperative chemotherapy with IAP (ifosfamide + epirubicin + cisplatin) regimen, the young patient was assessed as partial remission and received mastectomy and sentinel lymph node biopsy with the diagnosis of rhabdomyosarcoma. Final clear margin status was achieved for all cases.

As indicated in Tables 1 and 2, 7 patients received lumpectomy with R0 resection. Besides, 6 patients without recurrence underwent reexcision in our cancer center within 3 weeks for close margin confirmed after initial lumpectomy. The following indications would be evaluated before extended operation was performed: microscopic residue, large tumor size (>5 cm) and/or extended involvement in regional skin or muscle that unsuitable for breast conservative surgery, angiosarcoma with high grade. Ultimately, 31 patients (including those 6 reexcision) achieved negative margin after surgery, in which 14/38 underwent wide local resection and 17/38 received mastectomy. Axillary dissection was performed to 7 (7/38) patients, with 1 positive pathologic result.

Adjuvant chemotherapy was applied to 15 patients (15/38, 39.5%) according to different histologic types or clinical stages. The median tumor size of patients received chemotherapy was 4 cm (varying from 1.5 to 15 cm). Over half of them (7/15) were confirmed as angiosarcoma whereas others as extraskelatal osteosarcoma, Ewing sarcoma, spindle cell sarcoma, dermatofibrosarcoma protuberans, and dedifferentiated soft-tissue sarcoma. Owing to the advanced stage or high-risk recurrence rate, most of those patients (11/15) underwent the wide resection or mastectomy followed by chemotherapy. Recurrence was observed in 5 patients after chemotherapy. Three of them developed local or regional recurrence followed by distant metastases whereas other patients confirmed of metastasis as initial progression after chemotherapy and radiotherapy.

Total of 10 patients (10/38, 26.3%) received radiation therapy. Adjuvant radiotherapy was administered in 5 patients after local resection, 3 after mastectomy whereas other 2 patients took radiotherapy as salvage treatment. The median tumor size among patients received adjuvant radiotherapy was 5 cm. Angiosarcoma (5/8) was still observed as the most frequent subtype in patients who received postoperative radiotherapy. Three patients were found of regional relapse and one of them developed multisites metastasis. One patient, however, held a free local relapse interval of 7.5 months after initial lung metastasis.

TABLE 1. Clinicopathologic Characteristics and Treatment Modalities of 38 Patients With Primary Breast Sarcoma

Characteristics		No. of patients	n (%)
Patient age (year)	Median (ranges)	35 (16–70)	
Follow-up time (month)	Median (ranges)	40.19 (6–165)	
Menopausal status	Premenopausal	26	68.4%
	Postmenopausal	12	31.6%
Size of tumor	$\leq$4 cm	27	71.0%
	4 cm $<$ T $\leq$ 8 cm	9	23.7%
	$>$8 cm	2	5.3%
Lymph nodes	Positive	1	2.6%
	Negative	37	97.4%
Histologic type	Angiosarcoma	16	42.1%
	Dermatofibrosarcoma protuberans	5	13.1%
	Undifferentiated sarcoma	5	13.1%
	Pleomorphic fibrosarcoma	2	5.3%
	Liposarcoma	2	5.3%
	Rhabdomyosarcoma	2	5.3%
	Mixed and others*	6	15.8%
Histologic grade	Grade 1	10	26.3%
	Grade 2	22	57.9%
	Grade 3	6	15.8%
Surgical procedure	Local resection	7	18.4%
	Wide local resection	14	36.8%
	Mastectomy	17	44.8%
Axillary dissection	Yes	7	18.4%
	No	31	81.6%
Radiation therapy	Yes	10	26.3%
	No	28	73.7%
Chemotherapy	Yes	15	39.5%
	No	23	60.5%

PBS = primary breast sarcoma.
* Extraskelatal osteosarcoma, Ewing sarcoma, spindle cell sarcoma, myofibrosarcoma, adult fibrosarcoma and dedifferentiated soft tissue sarcoma each for 1 patient.

Locoregional Recurrence and Overall Survival

The local recurrences were found in 14 patients, and 11 patients (11/14) presented unifocal recurrence around the tumor bed, whereas the others were multifocal relapses in ipsilateral breast (Table 2). The patients with local recurrence would be recommended to receive surgery if operable to remove the tumor and then radiotherapy and/or chemotherapy according to histologic subtype and clinical condition. Six patients went through the recurrence for more than once. The average interval from initial treatment to locoregional recurrence was 97.9 ± 14.42 months (range 2–165 months). One-year and 3-year locoregional control (LRC) were 78.1% and 66.1%, respectively.

Eight patients developed distant metastasis, including lung (3/8), soft tissue of limbs (3/8) and bone (2/8), during the following time. With the entire cohort, OS at 1 year and 3 years were 100% and 89%, respectively. The average OS was 119.5 (range 20–165) months (Figure 1). As indicated in Figure 2, univariate analysis revealed that local recurrence free patients presented longer OS than those with recurrence (141 months versus 96.2 months, $P = 0.042$).

Angiosarcoma was identified as the most frequent subtype in PBSs in our study, which was consistent with other reports. Subgroup analysis of histology was analyzed based on 2 groups, angiosarcoma and nonangiosarcoma. Locoregional control of those 2 subgroups at 1 year and 3 years were 73.7%, 81.3% and 57.3%, 64.3%, respectively. There was no significant difference between 2 groups (as shown in Figure 3, $P = 0.737$). The similar outcomes occurred in OS (100%, 91.7% and 100%, 87.1%, respectively, $P = 0.530$) (Table 2 and Figure 3).

Prognostic Factors Analysis

The larger tumor size was the only clinical characteristic that associated with a decreased LRC and OS ($P = 0.014$ and $P = 0.000$, respectively) as shown in Table 2 and Figure 4. Aggressive surgical procedure like mastectomy did not bring extra benefits (Figure 5) regardless of the tumor size. Meanwhile, the age of first diagnosis, menopausal status, histologic type and grade, lymph nodes status, and adjuvant therapy were not found to be of any significance on univariate analysis for LRC or OS. The Cox proportional hazard model demonstrated that early recurrence could adversely affect OS [HR = 0.265; 95% confidence interval (0.071–0.988); $P = 0.048$] and the results were shown in Table 2 and Table 3.

DISCUSSION

Primary breast sarcomas are unusual diseases among all the breast malignancies. The peak incidence of PBSs was reported as 50 to 60 years old.[2,13] Although in our institution, the median age for the patients diagnosed as PBS was just 35

TABLE 2. Characteristics and Treatment Modality of Primary Breast Sarcoma: Univariate Analysis

Characteristics	No. of Patients	Survival Rate (%)		Median Survival in Months (Range)	*P* Value
		1 Year	3 Years		
Age				142 (80.4–203.6)	0.829
≤50	28	100	90.2	142	
>50	10	100	87.5	117 (53.2–180.8)	
Menopausal status					0.921
Premenopausal	26	100	89.5	117 (53.4–180.6)	
Postmenopausal	12	100	88.9	142	
Tumor size (cm)					<0.001
≤4 cm	27	100	94.7	142	
4 cm < T ≤ 8 cm	9	100	100	71	
>8 cm	2	100	50	20	
Histologic type					0.530
Angiosarcoma	16	100	91.7	-	
Others	22	100	87.1	117 (57.1–176.9)	
Histologic grade					0.754
Grade 1	10	100	87.5	-	
Grade 2	22	100	92.9	117 (38.2–195.8)	
Grade 3	6	100	80	-	
Surgical procedure					0.167
Local resection	7	100	62.5.	142	
Wide local resection and Mastectomy	31	100	96.2	165 (80.4–203.6)	
Axillary dissection					0.836
Yes	7	100	100	142 (45.9–238.1)	
No	31	100	96.4	117	
Local recurrence					0.042
Yes	14	100	74.6	117	
No	24	100	100	75 (37.6–112.4)	

PBS = primary breast sarcoma.

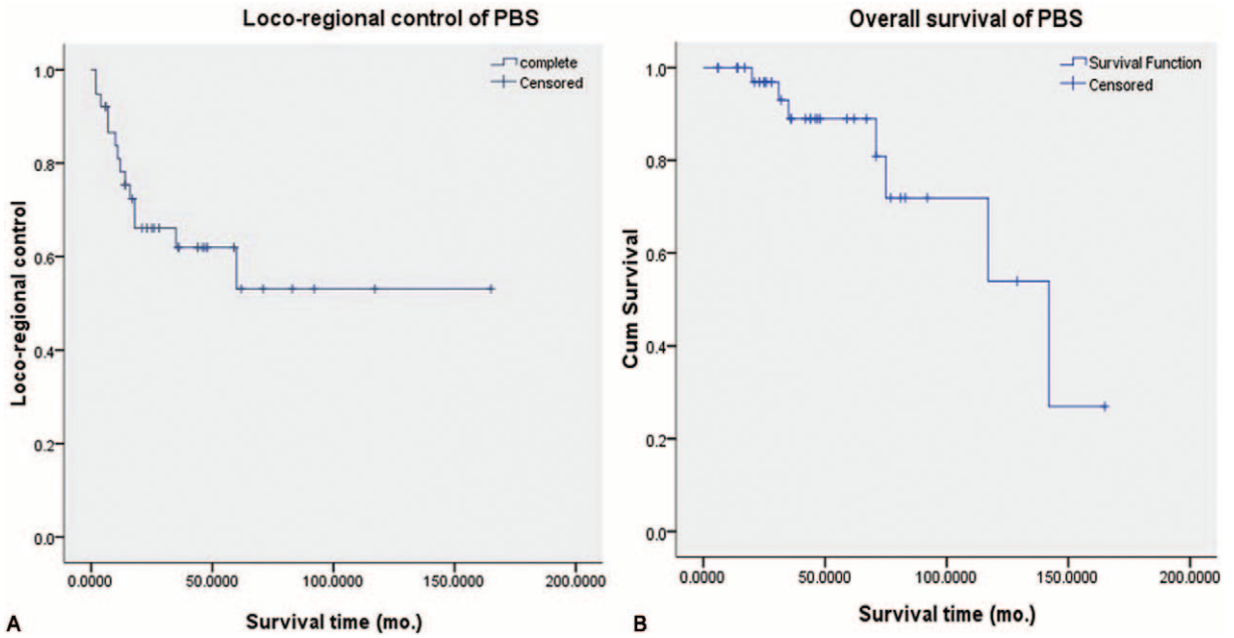

FIGURE 1. Kaplan–Meier probability curves of recurrence free survival and overall survival of primary breast sarcoma. Estimated 1-year and 3-year local control rate of 78.1% and 61.9%, respectively (A). Estimated 1-year and 3-year overall survival rate of 100% and 89%, with median survival time of 142 months (B).

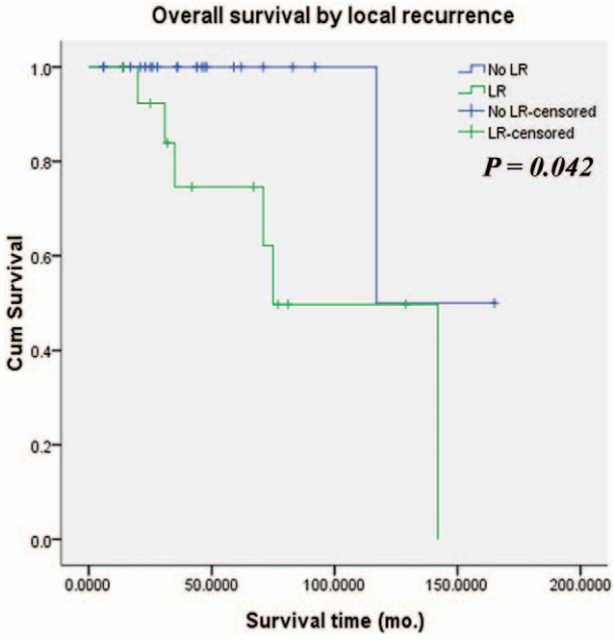

FIGURE 2. Kaplan–Meier plot of overall survival rate of patients with and without local recurrence during follow-up time ($P = 0.042$). LR: Loco-recurrence.

years old. It might be associated with relatively great proportion of patients diagnosed with angiosarcoma (16/38), which was generally diagnosed in the early age.[14,15]

With the rarity and diversity of PBSs, the evidence base for clinical management of breast sarcomas is less well developed than that for other cancers. Usually, treatment strategy is extrapolated from other locations of the soft-tissue sarcoma. As a general sense, the mainstay of sarcoma management is for surgery and the ultimate aim of surgery remains a complete surgical excision (R0) with a negative margin. Axillary lymph node dissection is unnecessary for patients with low risk of lymph nodes metastasis.[16] Nonetheless, several histologic subtypes, such as clear cell sarcoma, synovial sarcoma, angiosarcoma, and rhabdomyosarcoma, are considered associated with higher inclination to develop lymphatic metastasis. And sentinel lymph node biopsy was tentatively applied to help guide the regional therapy in selected subtypes of PBSs and other soft-tissue sarcomas other than invasive breast cancer. As for those aggressive and larger tumors, some researchers conjectured it might require a more aggressive surgical approach including radical resection and complex reconstruction.[9] As Mark[17] emphasized in early 1990s, tumor size and surgical margin status were important prognostic factors in fibrosarcoma of the head and neck. Compared with the tissue soft sarcomas in other sites, breast sarcomas confront relatively less challenges in processing anatomic structure. As shown in Figure 5, our study classified the local resection as lumpectomy with 1 cm surgical margin at least, and the results indicated there was no significant difference between local resection and wide local resection/mastectomy either for LRC or OS. In our series, a clear margin was achieved in all the cases regardless of the initial surgical types. Only 1 patient (2.6%) was confirmed as positive lymph nodes after axillary dissection, which was uncommon for involvement of regional nodes.[18] Generally, axillary dissection is not mandatory or routine in our institute. Because statistical analysis was limited by low percentage of that approach in our series, we descriptively presented some characteristics in patients underwent axillary dissection, such as large initial tumor size, inadequate surgical margin, aggressive histology and poor differentiation, and suspicious lymph nodes during preoperative examination. Yet, we could not draw further

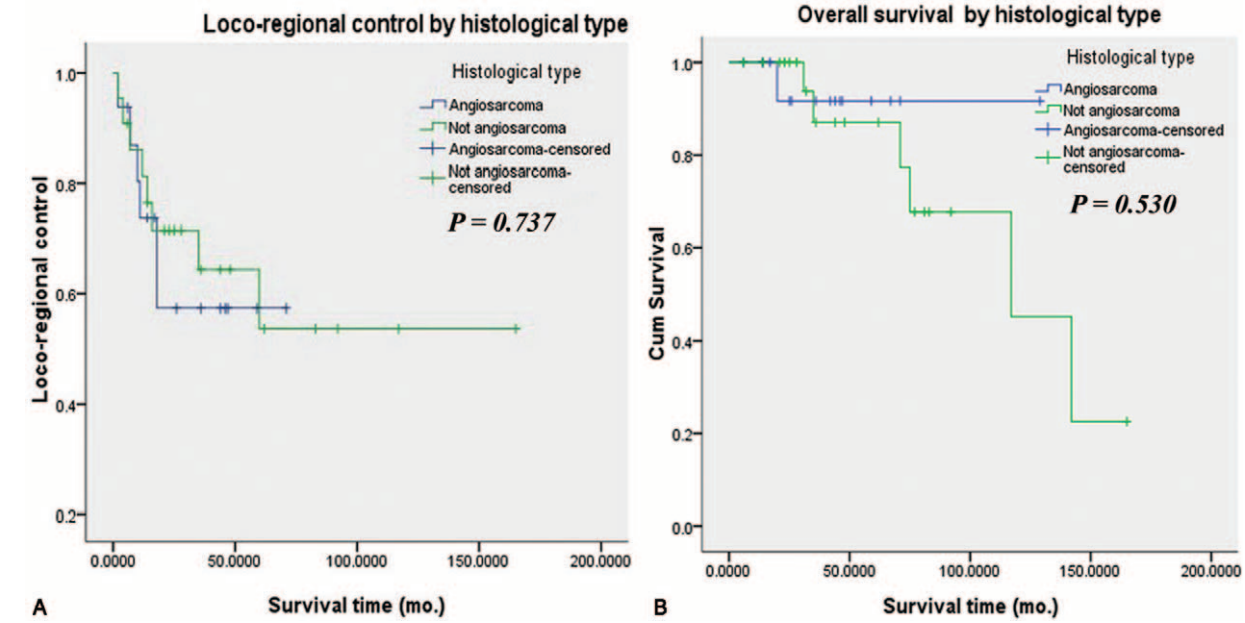

FIGURE 3. Locoregional control (A) and overall survival (B) by histologic type classified as angiosarcoma and nonangiosarcoma ones. Locoregional control rates at 1 year and 3 years were 73.7%, 81.3% and 57.3%, 64.3%, respectively ($P = 0.737$), whereas overall survival was 100%, 91.7% and 100%, 87.1%, respectively ($P = 0.530$).

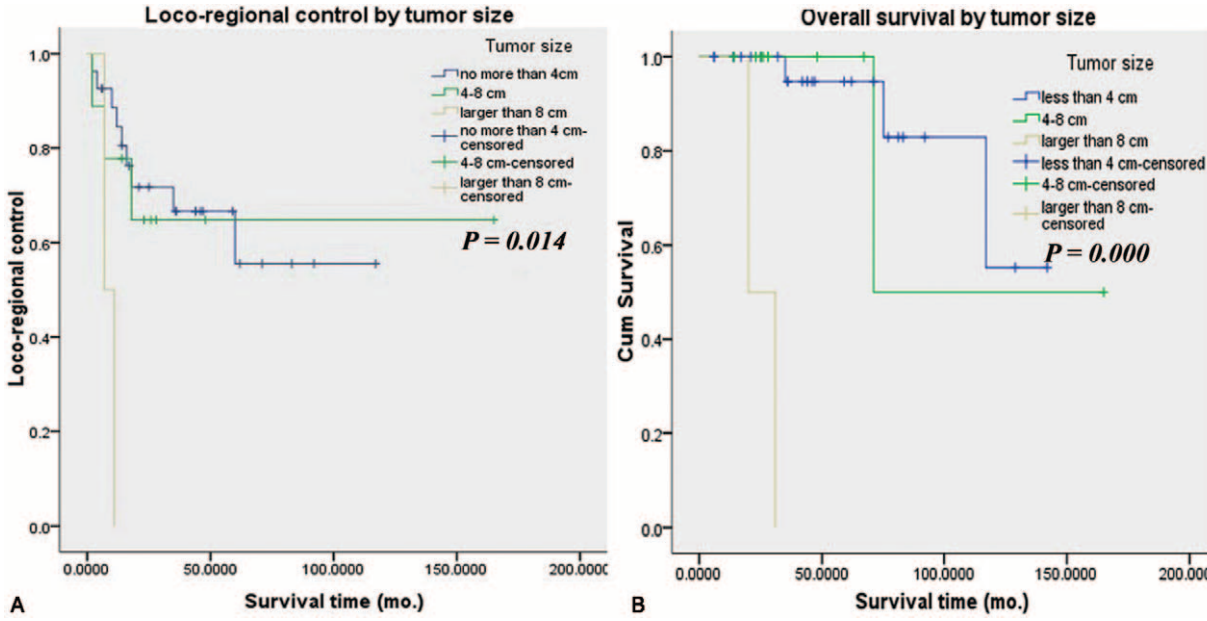

FIGURE 4. Kaplan–Meier plot of loco-regional recurrence control (A) and overall survival (B) of PBSs patients by tumor size. Larger tumor size significantly decreased the locoregional control ($P = 0.014$) and overall survival ($P = 0.000$). Tumor size is divided into 3 groups according to its maximum diameter as follow: $T \leq 4$ cm, 4 cm $< T \leq 8$ cm, $T > 8$ cm.

conclusion about definite indications for axillary dissection in PBSs. It was seen that type of surgery did not affect the prognosis as long as it reached the quality of margins.[13]

Because patients in the current study presented younger ages at diagnosis, organ preservation was of great significance in life quality improvements. Toesca et al[18] found that breast conservative surgery or reconstruction after mastectomy did not show a worse prognosis, compared with patients who underwent mastectomy, even in large proportion (91.9%) series of angiosarcoma. Thus, mastectomy might not be necessary if the safe surgical margin could be guaranteed.

Adjuvant radiotherapy for intermediate or high-grade soft-tissue sarcoma tends to improve local control and OS with benefit of organ functional preservation for patients with sarcoma.[19] The role of radiotherapy in PBSs, however, is still under debate. Some authors proposed that if negative surgical

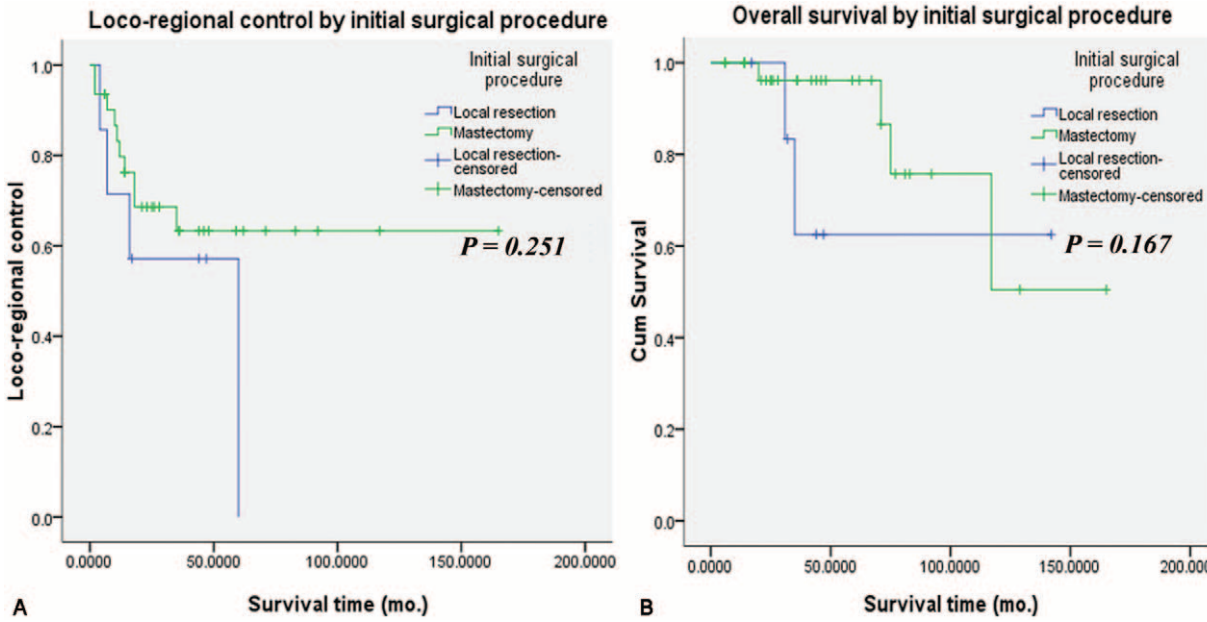

FIGURE 5. Locoregional control (A) and overall survival (B) by initial surgical procedure classified as local resection and mastectomy. Mastectomy did not improve either local control or overall survival ($P = 0.251$, $P = 0.167$, respectively).

TABLE 3. Summary of Multivariate Analysis For Potential Factors Associated With Overall Survival of Primary Breast Sarcoma

Characteristics	Associated *P* Value	HR (95% CI)
Tumor size	0.113	4.301 (0.707–26.154)
Histologic type	0.953	0.922 (0.061–13.822)
Histologic grade	0.604	1.55 (0.296–8.122)
Surgical procedure	0.907	0.851 (0.057–12.714)
Time to local recurrence	0.048	0.265 (0.071–0.988)
Time to distant metastases	0.493	1.405 (0.532–3.711)

PBS = primary breast sarcoma.

margins could be achieved, PBSs should be managed by conservative surgery with postoperative irradiation to improve LRC.[16] Even for the poor outcomes subtype as radiation-induced soft-tissue sarcoma, Riad[20] suggested that radiation would help improve the local control of the tumor ($P = 0.043$). Barrow et al[7] also indicated that adjuvant radiotherapy could decrease local failure from 34% to 13% in a series of 59 breast sarcoma patients. The similar result from Blanchard et al[21] also revealed a trend of survival benefit owing to adjuvant radiotherapy, but both of the studies failed to reach statistical significance. Limited by paucity of high-level evidence for systematic therapy in PBSs, we mainly follow the guideline of soft-tissue sarcoma in clinical practice. Adjuvant radiotherapy would be recommended if patients were confirmed with following indications: tumor size $\geq$5 cm; high histologic grade with close or positive surgical margin; boost radiotherapy recommended if reexcision could not be performed. With the limited number of patients receiving adjuvant radiotherapy, we did not find any difference between patients with or without radiotherapy. Besides, all patients in our series were confirmed as clear margin after initial operation or reexcision. Therefore, the importance of radiotherapy would be relatively minored.

As for adjuvant chemotherapy, though its role is disputable in sarcomas, some patients with particular subtypes might still benefit from chemotherapy, such as angiosarcoma, rhabdomyosarcoma, and synovial sarcoma.[22] Similar to soft-tissue sarcoma, adjuvant chemotherapy regimens in PBSs vary from one another according to different histology. In our institute, chemotherapy would be recommended in high-risk patients those who were confirmed as large tumor size, poor differentiation, positive or close surgical margin after final resection. The most frequent choice of regimen is adriamycin plus ifosfamide and mesna, especially in angiosarcoma and rhabdomyosarcoma subtypes. Etoposide and/or vincristine-based chemotherapy would be mostly applied in Ewing sarcoma.

In the locoregional failure pattern, it is found that most recurrence (8/14) presented near the original tumor bed area and only three patients (3/8) administrated with adjuvant radiotherapy. Two of those patients with tumor recurrence were tumor free after the salvage treatment. Besides, the Cox regression analysis suggested that early recurrence might bring worse OS in PBSs. Although the radiotherapy was not proved to improve the local control in our study, it might enhance regional control as a local treatment modality.

The rarity of PBSs precludes large samples and prospective study. Furthermore, the diversity of its histologic patterns leads to less consistency in prognostic factors results. As Table 4 shown, tumor size and grade, and the histologic subtype seemed relatively common in prediction of outcome. In the published retrospective studies, the most frequent breast sarcoma subtypes were described as angiosarcoma, liposarcoma, fivrosarcoma, and malignant fibrohistiocytoma.[13] As for histologic subtypes, it is found it was of no significance in univariate analysis. Because of the low incidence of PBSs and limited cases, we were not allowed to run subgroup analysis in systematic classification of histologic subtypes. We found angiosarcoma presented relative higher proportion in our series, which was consistent with previous report.[23] Therefore, in the subgroup analysis of pathologic pattern, all the cases were classified as angiosarcoma and nonangiosarcoma. Some authors suggested angiosarcoma of breast, especially radiation-induced angiosarcoma, tended to have worse clinical outcomes than other histologic subtypes.[13,15] Although the local recurrence control rate in patients with angiosarcoma in this study was low, compared with other histologic subtypes (73.7% versus 81.3% and 57.3% versus 64.3%, respectively), the difference did not reach the significance in either LRC or OS. Yet, it should cautiously draw conclusion and might need to get further verification with enlarged sample size and extended follow-up.

TABLE 4. Literature review

Authors (Published Year)	No. of Patients	Treatment	LRC%, (Time)	OS% (Time)	Prognostic Factors Identified
McGowan TS et al (2000)	78	SUR ± RT	75 (5 y)	57 (5 y)	Grade
Shabahang M et al (2002)	28	SUR	75 (10 y)	87.5 (10 y)	Margin
Zelek L et al (2003)	83	SUR ± (RT or chemo)	50 (10 y)	62 (10 y)	Grade, histologic subtype
Blanchard DK et al (2003)	55	SUR ± (RT or chemo)	45 (5 y)	57 (5 y)	ND
Malard Y et al (2004)	42	SUR	55–100 (10 y)	53–89 (10 y)	ND
Adem C et al (2004)	25	SUR ± (RT or chemo)	ND	66 (5 y)	Size
Bousquet G et al (2007)	103	SUR ± (RT or Chemo)	44 (5 y)	55 (5 y)	Margin, histologic subtype
Pencavel T et al (2011)	63	SUR ± (RT or Chemo)	42 (5 y)	37 (5 y)	Size, radiation history
Toesca A et al (2012)	37	SUR ± (RT or Chemo)	50.3 (5 y)	43.4 (5 y)	ND

Chemo = chemotherapy, LRC = locoregional control, ND = no data, No. = number, OS = overall survival, RT = radiotherapy, SUR = surgery, y = year.

As reported by Fields et al[5] tumor size >5 cm is a significant prognostic indicator of OS. A similar conclusion was drawn by the Mayo Clinic study.[24] Nevertheless, they both had pushed margins or infiltrative ones in those series. Because large tumor size tends to bring more technical difficulties during complete excision, presumably it is the surgical margin instead of tumor size that contributes to the clinical outcomes. In this study, we defined the cut-off value for tumor size as 4 cm and 8 cm, and found the larger tumor size just affected OS in the univariate analysis. The Cox regression revealed that the early recurrence was the only independent predictor for OS in PBSs. Because all the cases were verified as a negative margin, it was possible to reduce the chance of residual tumor after surgery regardless the primary tumor size.

Primary breast sarcomas are extremely rare types of tumors, and our data collection last over a relative long time. This study was limited by the short time and small number of cases from the single institution. Some histologic subtypes of tumor, such as high-grade angiosarcoma, radiation-induced breast sarcoma or undifferentiated sarcoma, present an aggressive feature especially after repeating recurrences. Therefore, it is necessary to confirm the current findings in a prolonged follow-up time.

CONCLUSIONS

Primary breast sarcomas are a group of rare, heterogeneous tumors, requiring for multimodality therapies. Surgery still plays an important role in treatment of PBSs. Yet, mastectomy is not superior to local resection if negative surgical margin could be achieved. Also, axillary lymph node dissection may not be necessary because of the low incidence of lymphatic metastasis. Sentinel lymph node biopsy, as an alternative treatment, could tentatively apply in specific histologic subtypes with higher propensity of regional lymphatic spread. Early tumor locoregional recurrence has an adverse effect on OS as it is only 1 factor that is associated with PBSs' prognosis. Proper adjuvant therapy following operation may be recommended to improve the local control and OS of this rare disease.

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