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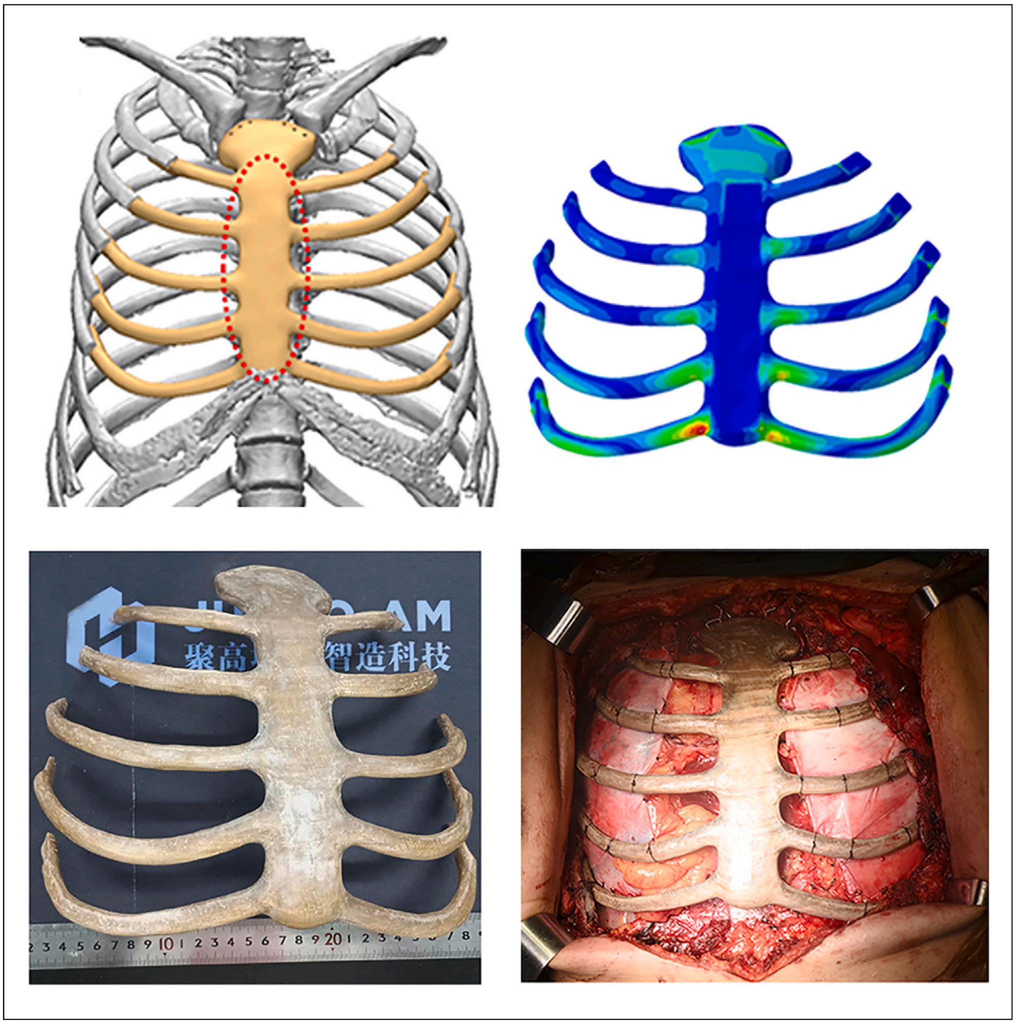

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Highlights

Chest wall sarcomas (CWS) should be treated as a malignant lesion with wide excision

Chest wall reconstruction using 3DP implants is an effective therapy for CWS

The tumor grade, size, and area have the potential to predict the prognosis of CWS

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Outcomes following the excision of sarcoma and chest wall reconstruction using 3D printed implant

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SUMMARY

The survival outcomes of patients with chest wall sarcomas (CWS) were evaluated after receiving wide excision and chest wall reconstruction by using three-dimensional printed (3DP) implants. The survival outcomes evaluating the effect of 3DP implants for chest wall reconstruction is lacking. Here, forty-nine patients with CWS underwent radical wide excision and chest wall reconstruction using 3DP implants. The surgical data and long-term survival outcomes were collected and analyzed. With a median follow-up of 36 months, the disease-free survival (DFS) and overall survival (OS) were 31.7% and 58.5%, respectively. In addition, the 3-year DFS and OS can be significantly differentiated using the classification criteria of tumor grade, tumor size tumor area. Hence, wide excision and chest wall reconstruction using three-dimensional printed implants are a safe and effective treatment for chest wall sarcoma. The novel classification criteria of tumor size and area have the potential to predict the prognosis of CWS.

INTRODUCTION

Primary chest wall sarcoma is rare disease in clinical practice, accounting for 15–20% of all sarcomas.[1] Chest wall sarcomas (CWS) can arise from bone and soft tissue, including osteosarcoma, chondrosarcoma, Ewing sarcoma, hemangiosarcoma, fibrosarcoma, synovial sarcoma, myofibroblastoma, and primary neuroectodermal tumor.[2] Wide excision is one of the most important treatments for CWS, while radiotherapy and chemotherapy have a low objective response rate to CWS.[3,4] It has been a great challenge to reconstruct chest wall defects after wide excision. In reality, the extent of wide excision is determined by the ability of chest wall reconstruction for most surgeons, including reconstruction implants, surgical techniques, and other factors.[4]

Due to the low incidence of CWS, it is difficult to carry out prospective, randomized clinical trials to investigate the clinical hypothesis.[4] Most current published studies are single-center retrospective studies with small sample sizes, and the patients were enrolled for a very long time, more than 30–40 years.[5–10] This inevitably leads to poor comparability of surgical techniques and treatment outcomes in some studies, which may result in contradictory conclusions. It is still difficult to find accurate prognostic factors for CWS. Otherwise, there are no specific TNM staging criteria for CWS to date. Only the 8th edition TNM staging criteria of bone tumors (trunk, extremities, skull, and maxillofacial) and soft tissue sarcomas (trunk and extremities) can be referred to develop an accurate postoperative staging.[11–13] However, there are many significant differences between the two staging systems, and many surgeons believe that the staging criteria are not suitable for CWS.[4]

Since 2015, we have focused on the wide excision of CWS and chest wall reconstruction using three-dimensional printed (3DP) implants.[14–19] 3DP technology can help produce individual implants with biomechanics matching those of cortical bone for chest wall defects.[16,19] Furthermore, we performed a "sandwich" chest wall reconstruction using 3DP implants, including pleura, 3DP implant, and musculocutaneous flap reconstruction.[14–19] One hundred and fourteen patients received surgery to reconstruct chest wall defects, forty-nine of whom suffered from CWS. Herein, all patients were enrolled in three years and underwent a consistent surgical protocol, meaning that surgical techniques and treatment outcomes were more comparable in this study. With a median follow-up of 36 months, 57.1% of patients experienced recurrence, and 34.7% of them died of CWS. The main clinical results, surgical complications, recurrence, and survival data are presented in the following chapters, and the disease-free survival (DFS) and overall survival (OS) are further analyzed.

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Table 1. Characteristics of 49 patients with chest wall sarcomas

	N	%
Age		
Median/Range	58.00/15-78	
Sex		
Male/Female	22/27	44.9/55.1
Location		
Sternum/Ribs	19/30	38.8/61.2
Symptoms		
Palpable mass	28	57.1
Asymptomatic	11	22.4
Pain	8	16.3
Dyspnea	1	2.1
Weight loss	1	2.1
History of disease		
Initial disease	30	61.2
Recurrent disease	19	38.8
Tumor dimensions		
Average maximum diameter (Dt)	9.2 ± 4.6	
Average maximum area (St)	88.1 ± 94.1	
Chest wall defect dimensions		
Average maximum diameter (Dd)	13.3 ± 4.8	
Average maximum area (Sd)	168.8 ± 148.2	
Coefficient of chest wall defect		
Dd/Dt	1.6 ± 0.6	
Sd/St	2.9 ± 2.3	
Tumor grade		
Low	30	61.2
High	19	38.8
Pathology		
Chondrosarcoma (low/high grade)	16 (9/7)	32.7
Ewing sarcoma	1	2.1
Osteosarcoma	2	4.1
PNET	2	4.1
Desmoid tumor	8	16.3
Liposarcoma	2	4.1
Leiomyosarcoma	4	8.2
Fibrosarcoma	4	8.2
Synovial sarcoma	2	4.1
Myofibroblastic tumor	3	6.1
Pleomorphic sarcoma	2	4.1
Other sarcoma	3	6.1

RESULTS

Patients and clinical presentation

Forty-nine patients with CWS underwent wide excision and chest wall reconstruction using 3DP implants. Of these, nine patients underwent surgery at an outside institute. The patient characteristics are shown in Table 1. There were 22 males (44.9%) and 27 females (55.1%), with a median age of 58 years. Most patients were symptomatic, with examination finding a palpable mass (57.1%) and the symptom being pain

Table 2. Clinical characteristics, surgical resection, and multimodality treatments

	No of Patients (n = 49)	%
Resection		
Sternum	19	38.8
Partial	10	20.4
Complete	9	18.4
Ribs (average number)	30 (3.6)	61.2
Adjacent organs		
Lung	4	8.2
Pericardium	1	2.0
Clavicle	2	4.1
Vertebrae	1	2.0
Surgical margin status		
R0	45	91.8
R1	4	8.2
3DP Implant shape		
Horizontal type rib	22	44.9
E type rib	4	8.2
Vertical type rib	4	8.2
Whole sternum	6	12.2
Inferior segment sternum	5	10.2
Upper segment sternum	8	16.3
Reconstruction		
Mesh + 3DP implants	43	87.7
Mesh + 3DP implants + musculocutaneous flap	6	12.3
Complications		
Mortality (30 days)	0	0
Surgical site infection	3	6.1
Pneumonia	3	6.1
Implant migration	2	4.1
None	41	83.7
Neoadjuvant therapy		
Chemotherapy	6	12.2
Radiotherapy	5	10.2
None	38	77.6
Adjuvant therapy		
Chemotherapy	12	24.5
Radiotherapy	4	8.2
None	33	67.3
Recurrence		
Yes	28	57.1
No	21	42.9
Site of recurrence		
Chest wall	10	20.4
lung	12	24.5
Other organs	6	12.2
Tumor related death		

(*Continued on next page*)

Table 2. *Continued*

	No of Patients (n = 49)	%
Yes	17	34.7
No	32	65.3

(16.3%). Nineteen patients (38.8%) had recurrent CWS and previous surgical interventions before this visit. The main lesions were located at the sternum in nineteen patients, while the others were mainly in the ribs.

Tumor characteristics

The resected CWS were evaluated for pathology, grade, and size (Table 1). The average diameter (Dt) and area (St) of the maximum cross-section of tumor were 9.2 cm and 88.1 cm^2, respectively. Meanwhile, the chest wall defects were measured together in the resected samples. The average diameter (Dd) and area (Sd) of chest wall defects were 13.3 cm and 168.8 cm^2, respectively. To further evaluate the relationship between CWS and chest wall defects, the coefficients of chest wall defects were defined as Dd/Dt and Sd/St with values of 1.6 and 2.9, respectively. Pathological subtypes are shown in Table 1. Bony and soft tissue sarcomas accounted for 38.8% and 61.2%, respectively. Bony sarcomas included chondrosarcoma, Ewing sarcoma, and osteosarcoma. More subtypes of soft tissue sarcomas were observed, including liposarcoma, leiomyosarcoma, fibrosarcoma, synovial sarcoma, and desmoid tumor. There were eight (16.3%) desmoid tumors in this study. Pathological differentiation of the whole tumors showed low- or intermediate-grade (61.2%) and high-grade (38.8%) sarcomas.

Tumor resection and chest wall reconstruction

All patients underwent full-thickness wide excision to obtain enough surgical margin, including skin, muscle, skeleton, and adjacent organs. The details of surgical resection and reconstruction are described in Table 2. Partial or complete resection of the sternum was performed in 19 patients (38.8%). An average of 3.6 ribs were resected in 30 patients (61.2%). Four patients underwent wedge resection of the lung, while local excisions of adjacent organs, including the pericardium, clavicle, and vertebrae, were performed in 4 patients. In all, R0 surgical margins were obtained in 45 patients, accounting for 91.8%. Programmed chest wall reconstruction surgery was performed to repair the chest wall defects. The 3DP PEEK implants were fabricated as six subtypes,[19] including horizontal type rib, E type rib, vertical type rib, whole sternum, upper segment sternum, and inferior segment sternum (Figure 1). 3DP implants were fixed to the residual sternum or ribs to repair the bony structure in the middle layer (Figure 2).[18,19] Then, the biological mesh was continuously sutured with residual pleura in the innermost layer. Forty-three patients had enough skin and muscles to cover the implants and suture the surgical incision, but 6 patients with large soft tissue defects had to receive a musculocutaneous flap to cover the wound, including 4 with a latissimus dorsi flap, 1 with a pectoralis major myocutaneous flap, and 1 with a rectus abdominis musculocutaneous flap.

There were no 30-day perioperative or hospital mortalities. With respect to surgical complications, surgical site infections, pneumonia, and implant migration occurred most commonly in this study. Three patients suffered from pneumonia, requiring extra treatment. Surgical incision infections developed in 3 patients in 6–12 months after surgery because the skin and subcutaneous tissue on the implant were too thin to withstand the large incision tension. Of these, two patients developed wound infections after receiving neoadjuvant radiation or adjuvant radiation. Two patients required surgical debridement with mesh and 3DP implants removal 1 year after surgery, and a pectoralis major myocutaneous flap was placed on the wound after vacuum sealing drainage in the wound for 2 weeks. Chronic inflammation of wounds over approximately one year stimulates the formation of dense pleural fiberboards, which can support the chest wall and prevent abnormal breathing. The other patient required secondary wound closure suturing after adequate cleaning and dressing of surgical site infections. When the skin defect is large, or the incision tension is high, using musculocutaneous flap to cover the implant is a better choice. Two patients suffered from 3DP implant migration in the residue rib junction due to the recurrence of tumor in this site.

Disease-free survival and overall survival

In general, patients with low-grade soft tissue sarcomas and conventional chondrosarcomas were resected without induction therapy. Ewing sarcomas, osteosarcomas, and dedifferentiated or mesenchymal chondrosarcomas were treated with neoadjuvant chemoradiation or chemotherapy alone. In all, 22.4% of patients received neoadjuvant therapy before surgery, while 32.7% of patients received adjuvant therapy after surgery. Doxorubicin and ifosfamide were the main chemotherapy regimens, and a dose range of 45–60 Gy was given to patients with high-grade CWS. Over a median follow-up of 36 months, 28 patients (57.1%) experienced recurrence, and 17 of them (34.7%) died of CWS. Local recurrence and metastasis were detected in 20.4% and 36.7% of patients, respectively. Lung metastasis was the predominant pattern of recurrence. In addition, 8 patients with desmoid tumors had no recurrence or death in the follow-up period, which can be attributed to the low malignancy of the tumor and wide excision. Thus, desmoid tumors were excluded from other sarcomas in the following survival analysis. 16 patients suffered from chondrosarcoma of the chest wall, accounting for the highest number of all subgroups. The subgroup of chondrosarcoma was analyzed in the following study.

The 3-year disease-free survival and overall survival after the wide excision of CWS for variables are described in Table 3, including age, sex, tumor location, tumor grade, history of disease, histology, Dd/Dt, Sd/St, margin status, and neoadjuvant and adjuvant therapy. The 3-year disease-free survival and overall survival for 41 patients with CWS were 31.7% and 58.5%, respectively. Table 3 describes significant favorable

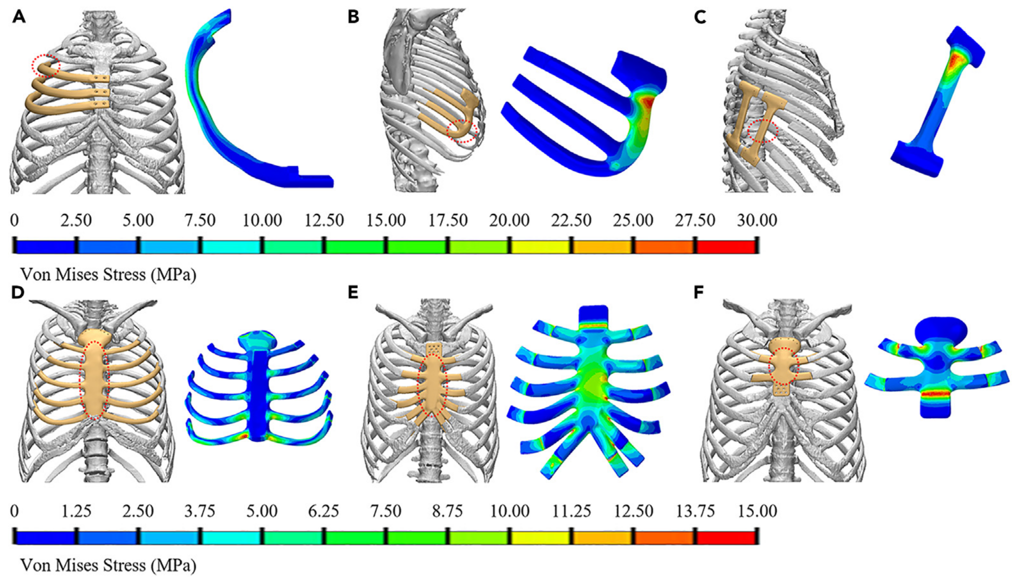

Figure 1. The design and von Mises stress of the implant for chest wall reconstruction

(A) In-suit rib reconstruction; (B) costal arch reconstruction; (C) vertical reconstruction; (D) whole sternum reconstruction; (E) inferior segment sternum reconstruction; (F) upper segment sternum reconstruction.[19]

prognostic variables for 3-year disease-free survival, which included initial disease, low tumor size and area, low tumor grade, Dd/Dt > 1.4, and Sd/St > 2.0. Favorable prognostic factors for overall survival included low tumor size and area, low tumor grade, Dd/Dt > 1.4, and Sd/St > 2.0. The maximum diameter of the tumor was divided into three subtypes, including 0–6 cm, 7–11 cm, and ≥12 cm, while the maximum area of the tumor was classified as 0–30 cm^2, 31–90 cm^2, and ≥91 cm^2. The 3-year disease-free survival and overall survival can be significantly differentiated according to the above classification standard (Figures 3 and 4). The coefficients of chest wall defects (Dd/Dt; Sd/St) can be considered simple prognostic factors for CWS (Figures 3 and 4), especially in the assessment of surgical resection extent, because the coefficients can be easily obtained and calculated during surgery. The margin status showed no prognostic role due to the limited number of R1 margins (Table 3). Tumor grade showed a favorable prognostic role in all sarcomas. The 3-year DFS and OS can be significantly differentiated according to tumor grade in the chondrosarcoma subgroup and other sarcomas subgroup (Figures 3E, 3F, 4E, and 4F). In addition, the prognostic roles of tumor grade for 3-year disease-free survival and overall survival were more obvious in newly diagnosed patient (DFS, log rank $p < 0.001$; OS, log rank $p = 0.002$) than in the recurrent patients (DFS, log rank $p = 0.081$; OS, log rank $p = 0.051$). In stratification analysis in the chondrosarcoma subgroup (16) and other sarcomas subgroup (25), history of disease, histology, tumor size and area, margin status had no prognostic role for DFS and OS due to the limited sample number.

DISCUSSION

Wide excision is the most common treatment for chest wall sarcoma. However, it is a great challenge to repair large chest wall defects. One of the important reasons is the lack of appropriate implants, especially in the sternum and costal arch. 3DP technology can produce personalized implants with anatomically matching shapes and properties that are more suitable for repairing irregular anatomic structures.[20–23] Compared with the 3DP process of titanium implants, the FDM craft of PEEK material has more advantages in implant manufacturing, including shorter fabricating times (<72 h), better matching of mechanical properties (80–90 MPa), and lower production costs.[19] In our previous study,[15] pulmonary function was maximally reserved by using 3DP PEEK implants to repair chest wall defects, and the forced vital capacity of patients decreased only 15% after surgery, while other pulmonary function indices showed no change. In this series, we designed six subtypes of implant shapes for chest wall reconstruction, and it has been proven that all implants can match the chest wall defect individually. R0 resection was achieved in 91.8% of patients. R1 resection mainly occurred in tumors adjacent to the spine, heart, and great vessels. Given the surgical risk and difficulty of reconstruction, the R1 margin status can be acceptable in these cases.[4] In this series, the 2 spare implants with a larger size were used in surgery due to the R1 margin.

Due to the low incidence of CWS, it is difficult for clinicians to accumulate sufficient treatment experience with CWS. It is worth noting that most of the published reports on CWS are single-center, retrospective studies with a very long-time span.[4–10] It is possible that the surgical procedures used in the same study varied greatly. In this study, 49 patients with CWS underwent the same surgical procedures over 3 years, which made the clinical data more comparable. With a median follow-up of 36 months, 28 patients (57.1%) experienced recurrence, and 17 of them (34.7%) died due to CWS. The recurrence rate of initially diagnosed patients was significantly lower than that of patients with a recurrent disease, but the overall survival was not related to the history of disease. Otherwise, distant metastasis, especially lung metastasis, was the predominant recurrence pattern rather than local recurrence in this series. Robert and colleagues reported the similar recurrence patterns of

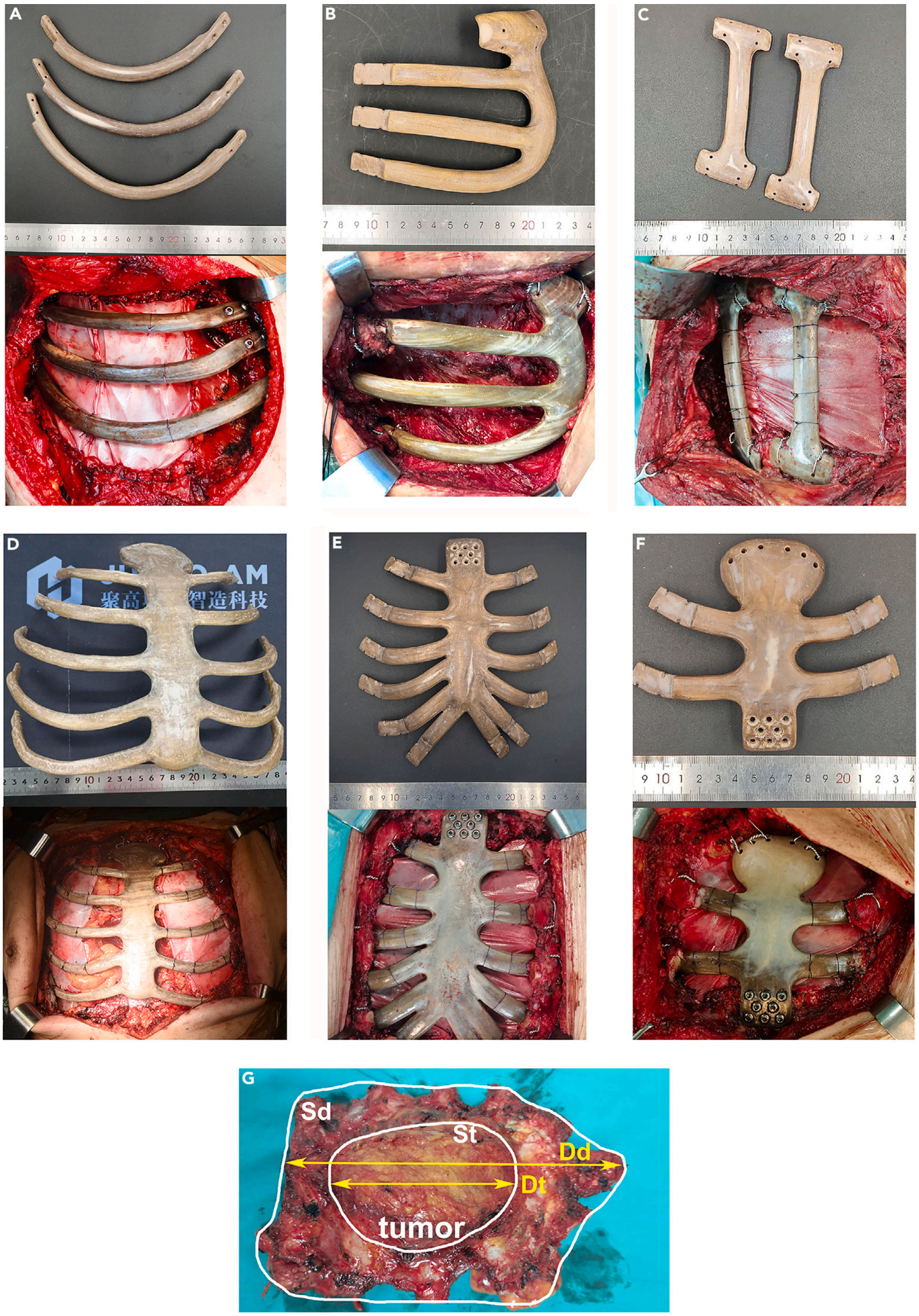

Figure 2. The application of 3DP PEEKimplants in chest wall surgery

The 3DP PEEK implants and corresponding surgery images of horizontal type ribs (A), E type ribs (B) and vertical type ribs (C). The 3DP PEEK implants and corresponding surgery images for whole sternum (D), inferior segment sternum (E), and upper segment sternum (F). The coefficients of chest wall tumor and defects (G), Dt, Diameter of tumor; Dd, Diameter of defect; St, area of tumor; Dd, area of defect.[18,19]

Table 3. Three-year disease-free and survival data after chest wall tumor resection (N = 41, excluding desmoid tumor)

	N	3-year disease-free survival (%)	Log rank p value	3-year overall survival (%)	Log rank p value
Age					
>58	21	42.9	NS	71.4	NS
≤58	20	20.0		45.0	
Gender					
Male	21	38.1	NS	57.1	NS
Female	20	25.0		60.0	
Location					
Sternum	19	26.3	NS	63.2	NS
Ribs	22	36.4		54.5	
History of disease					
Initial	25	48	0.006	64.0	NS
Recurrent	16	12.5		50.0	
Histology					
Bony	19	42.1	NS	57.9	NS
Soft tissue	22	22.7		59.1	
Tumor grade					
Low grade	22	59.1	<0.001	86.4	<0.001
High grade	19	5.3		26.3	
Tumor grade of Chondrosarcoma					
Low grade	9	77.8	0.009	77.8	0.049
High grade	7	14.3		28.6	
Maximum tumor diameter (Dt)					
0–6 cm	14	50.0	0.004	85.7	0.014
7–11 cm	17	29.4		52.9	
≥12 cm	10	10.0		30	
Maximum tumor area (St)					
0–30 cm^2	14	50.0	0.012	85.7	0.010
31–90 cm^2	14	28.6		57.1	
≥91 cm^2	13	15.4		30.8	
Dd/Dt					
<1.4	20	10.0	0.001	30.0	<0.001
>1.4	21	52.4		85.7	
Sd/St					
<2	17	5.9	<0.001	29.4	0.002
>2	24	50.0		79.2	
Margin status					
R0	38	31.6	NS	34.2	NS
R1	3	33.3		33.3	
Neoadjuvant therapy					
Yes	11	36.4	NS	54.5	NS
No	30	30.0		60.0	
Adjuvant therapy					
Yes	16	31.3	NS	56.3	NS
No	25	32.0		60.0	

Dd, maximum defect diameter; Sd, maximum defect area; NS, not significant.

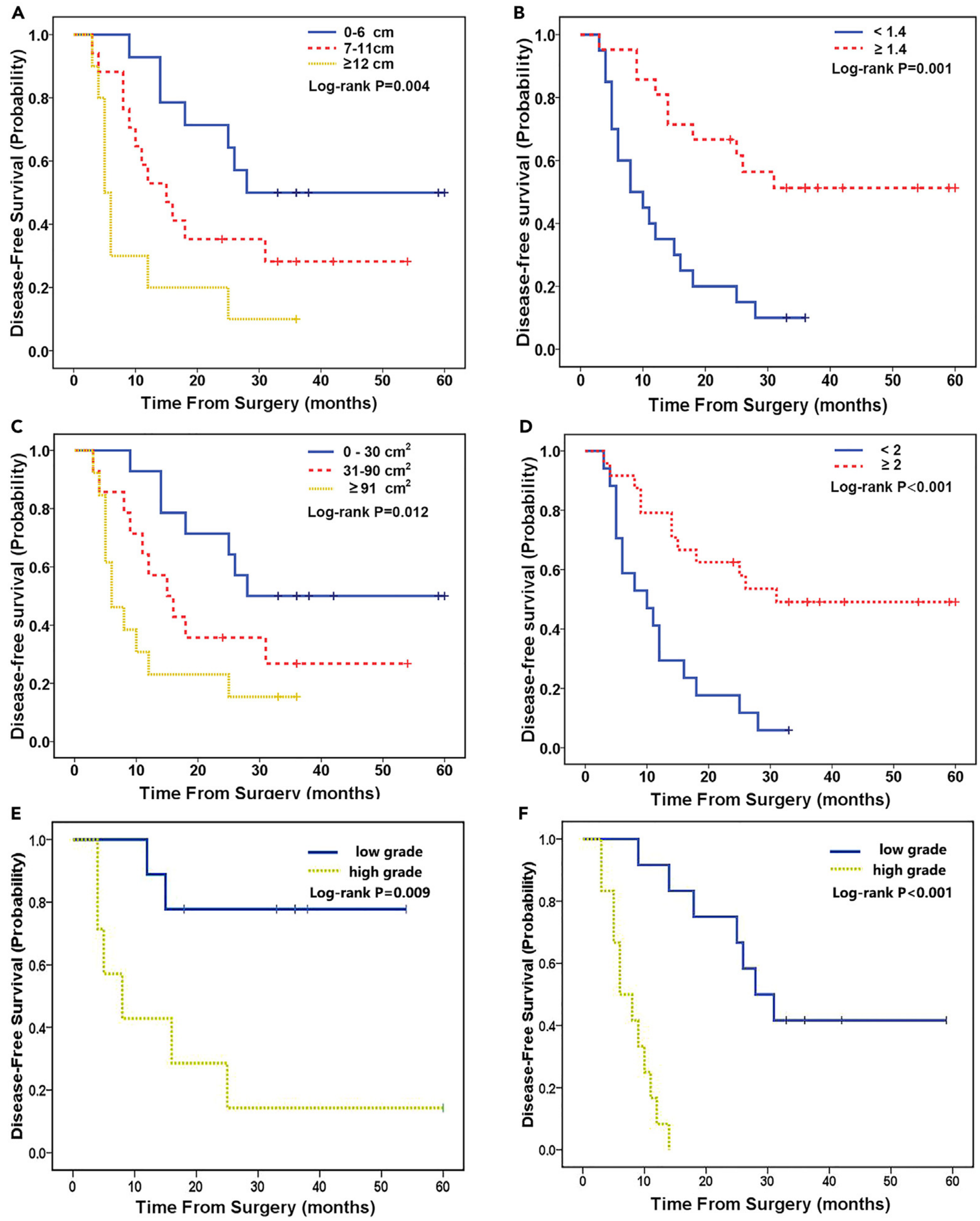

Figure 3. The disease-free survival of 41 patients after surgery

Disease-free survival of 41 patients with CWS in the subgroup of tumor size (A), Dd/Dt (B), tumor area (C) and Sd/St (D), tumor grade of Chondrosarcoma (E) and other sarcomas (F).

CWS in 45 patients.[24] Only 32.7% of patients received adjuvant chemotherapy or radiotherapy after surgery. Adding neoadjuvant or adjuvant therapy might reduce the rate of metastasis, although most CWS are not sensitive to chemoradiotherapy.[6,7,25] Patients with Ewing sarcoma of the chest wall can obtain better survival with neoadjuvant or adjuvant therapy[26]; however, the prognostic role of neoadjuvant or adjuvant therapy for other sarcomas is controversial in previous studies.[7,25]

To date, there are no TNM staging criteria specifically for CWS. The 8th edition TNM staging criteria of bone tumors and soft tissue sarcoma can be used to identify the stage of CWS. However, there are many differences between the two staging systems, especially the T staging criteria. In the main reference cited by the NCCN guidelines, CWS was combined with sarcoma of the trunk and extremities due to a small sample size.[13] In most studies[9,24,27–30] on soft tissue sarcoma of the chest wall, the classification criteria for tumor size were defined as ≥5 cm and <5 cm, which may refer to the NCCN guidelines of soft tissue sarcoma. However, the long-term survival outcomes of the two subgroups were inconsistent in these studies.[24,27–30] Nakahashi reported a classification standard of soft tissue sarcoma size (>7.05 cm and <7.05 cm),

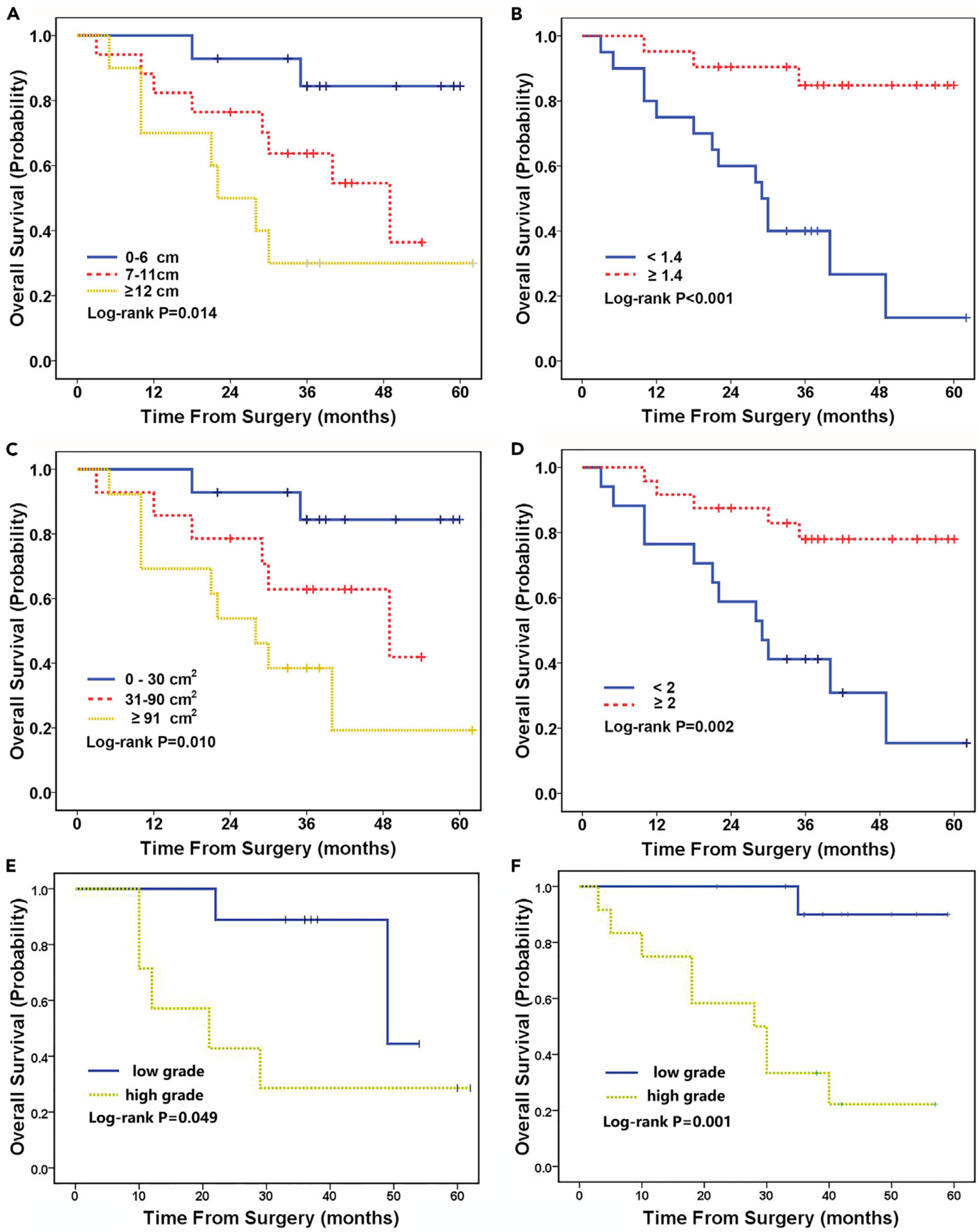

Figure 4. The overall survival of 41 patients after surgery

Overall survival of 41 patients with CWS in the subgroup of tumor size (A), Dd/Dt (B), tumor area (C) and Sd/St (D), tumor grade of Chondrosarcoma (E) and other sarcomas (F).

and there was a significant difference in OS but no difference in DFS.[8] In a study on chest wall Ewing sarcoma, the tumor size was divided into >6 cm and ≤6 cm, but the OS and DFS could not be significantly distinguished in the subgroups.[26] Collaud and colleagues used the TNM staging criteria for bone tumor and soft tissue sarcoma to identify the clinical stage of CWS, but the long-term survival outcome had no relationship to the T stage.[9] In this study, we did not differentiate CWS into bone tumors and soft tissue sarcomas and excluded desmoid tumors due to the low malignant potential. In the 41 patients with CWS, the diameter of the tumor was divided into 0–6 cm, 7–11 cm, and ≥12 cm, and the 3-year DFS and OS of these patients were significantly different in the three subtypes.

To further evaluate the prognostic factors of CWS, the area of the tumor was also classified as 0–30 cm^2, 31–90 cm^2, and ≥91 cm^2 in this study. The 3-year DFS and OS can be significantly differentiated using the area of the tumor. The tumor area can be accurately calculated in the assessment of pathologic diagnosis, and it may be more objective and complex than the tumor size. Kachroo et al. used tumor volume to assess the tumor grade, and tumor volume ≤ 200 cm^3 was proven to be a prognostic factor for CWS.[7] However, it is difficult to calculate the tumor volume accurately because of the irregular shape of the tumor. Therefore, we further calculated the diameter ratio of defect (Dd) and tumor (Dt), the area ratio of defect (Sd) and tumor (St), to evaluate the prognostic value. Dd/Dt > 1.4 or Sd/St > 2.0 were prognostic factors for CWS, and the 3-year DFS and OS can be significantly differentiated. Compared with the margin distance, the value of Dd/Dt or Sd/St was easy to calculate in surgery and can be used as a standard for wide excision. The tumor grade was another effective predictor of prognosis for CWS in this series. The patients with low tumor grade can get a longer 3-year DFS and OS, especially for the newly diagnosed patients. The 8 patients with desmoid tumor did not recur in the following period and it is suggested that wide excision is an effective treatment for this aggressive tumor. Although many studies suggested that the margin status and resection thickness was not associated with desmoid tumor recurrence, most surgeons agreed that desmoid tumor of the chest wall should be treated as a malignant lesion with Wide excision.[4] Wide excision with above 2 cm margin distance should be attempted to obtain an R0 resection margin. For the 16 patients with chondrosarcoma, tumor grade was the only effective predictor of prognosis. Other variables, including history of disease, histology, Dd/Dt, Sd/St, margin status, and neoadjuvant and adjuvant therapy, had no prognostic role for DFS and OS due to the limited sample number.

Limitations of the study

Some limitations of this study must be indicated herein. First, similar to most studies of CWS, this is a retrospective study with a small sample size, which can be attributed to the low incidence of CWS. Second, 3DP PEEK implants, unlike titanium alloy, cannot be cut during surgery. Accurate three-dimensional reconstruction of CT images is necessary to evaluate the excision extension of CWS and the size of implants. Therefore, it is important for doctors and engineers to work closely together. Third, surgical site infection was the main perioperative complication in this series, which may be related to poor integration between 3DP PEEK implants and soft tissues. Surface modification of PEEK implants can increase soft tissue integration and reduce surgical complications in animal experiments.[31]

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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AUTHOR CONTRIBUTIONS

Lei Wang: conceptualization, methodology, software, validation, investigation, visualization, resources, writing-original draft, and project administration. Xiaolong Yan and Jing Li: surgery, investigation, data curation, and review and editing. Jinbo Zhao, Sanhu Yang, and Jian Wang: investigation and writing-review and editing. Dichen Li and Changquan Shi: software and writing-review and editing. Shaoming Li and Junqi Wang: methodology, writing-review and editing, and supervision. Tao Jiang and Lijun Huang: conceptualization, methodology, formal analysis, investigation, resources, writing-review and editing, visualization, and project administration.

DECLARATION OF INTERESTS

The authors have declared no competing interests.

INCLUSION AND DIVERSITY

We support inclusive, diverse, and equitable conduct of research.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Critical commercial assays		
Surgical PEEK materials	(Wang et al.)[15]	https://invibio.com/en/materials-solutions/implantable-peek
Pericardial patch	(Wang et al.)[15]	http://www.guanhaobio.com/index.php?c =industrial&a=index&id=829
Software and algorithms		
Materialise Mimics 16.0	(Kang et al.)[16]	https://www.materialise.com/en/healthcare /mimics-innovation-suite/mimics
Other		
fused deposition modeling 3D printed machine (Jugao-AM-Doctor)	(Wang et al.)[19]	http://jugaozengcai.com/show-57.html

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources and reagents should be directed to and will be fulfilled by the lead contact, Lei wang (tuodi1986@126.com).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- Data reported in this paper will be shared by the lead contact upon request.
- This paper does not report original codes.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Experimental models

Patients with primary or recurrent CWS were referred to our department from December 2016 to October 2019. First, all patients underwent fine needle aspiration biopsy to obtain a pathologic diagnosis. Then, positron emission tomography computed tomography and bone scintigraphic imaging were performed to identify the existence of distant metastasis in other organs. The patient was enrolled in the study if the expected diameter of the chest wall defect was over 5 cm. A total of 49 patients with CWS were selected for the study, including 22 males and 27 females, with an average age of 58 years, ranging from 15 to 58 years old. The study was approved by the Institutional Ethics Committee of the Fourth Military Medical University (IRB number: TDLL-201710-09). All patients volunteered to participate in the study and signed informed consent forms.

METHOD DETAILS

Surgical planning

All of the 3DP implants in this study were supplied to the patients for free. Computed tomography (CT) images with slice thickness at 1.00 mm were obtained by using a 64 detector CT scanner (GE LightSpeed VCT) for all patients. CT scan image output in DICOM format was exported to 3D visualization software (Mimics software, version 16.0, Materialise, Inc., Leuven, Belgium) for surgical planning. The prospective resection margin was estimated as a minimum distance of 3 cm beyond the cancer. 3DP implants were designed and made to simulate the same shape as the bony structure of the patient.

Three-dimensional printed implants

All of the 3DP implants in this study were supplied to the patients for free. To make an R0 wide excision, the dimensions of the 3DP implants were designed up to at least 3 cm apart from the anticipated resection margin. In our previous study,[16,19] 3DP implants were grouped into six subtypes to carry out individualized chest wall reconstruction. As shown in Figure 1 in our previous study,[19] the 3DP implants for rib reconstruction could be categorized into three types based on the position. The implant was designed as the rib shape if the chest wall defect occurred in the anterior and lateral chest walls (Figure 1A). Special implant shapes, including the E type (Figure 1B) and vertical type (Figure 1C), were used to reconstruct the costal arch and the defect adjacent to the spine. The 3DP sternum implants could also be divided into three types: whole sternum (Figure 1D), upper segment sternum (Figure 1E), and inferior segment sternum (Figure 1F). In some special parts, such as costal arch and the defect adjacent to the spine, we always prepare a spare implant with a larger size in case the implant can not match the defect. The spare implant with a larger size would be used if the positive margin was found in the surgery. The manufacturing crafts of 3DP PEEK implants have been presented in our previous studies.[19] In brief, a fused deposition modeling (FDM) 3DP machine (Jugao-AM-Doctor, Xi'an Jiaotong University, melting temperature, 340°C) was used to fabricate these PEEK implants. According to previous and finite element analysis (FEA) data, the junction parts of the PEEK implant were relatively weak strength areas. Thus, the vulnerable part and junction part were strengthened, while some rigid parts were weakened in the manufacturing process. All materials were assumed to be homogeneous, isotropic, and linear elastic. In addition, the implants were processed in a surgical grade manner, including ultrasonic cleaning, ethylene oxide sterilization and disinfection monitoring.

Surgical technology

Forty-nine patients suffered from CWS, including 30 with rib tumors and 19 with sternum tumors. All patients underwent wide excision of the tumor followed by a large chest wall defect. The proximal pleura and muscles were wholly removed simultaneously. The disease-free resection (R0) margin was established during the operation on the basis of frozen tissue section analysis. An average of 6–8 samples were gathered in the surgical margin, including skin, muscles, and subcutaneous fatty tissues. The chest wall defect needed to be repaired like a "sandwich model", involving the reconstruction of the pleura, bones and muscles. As shown in Figure 2 in our previous study,[19] for patients with ribs defects in anterior chest wall, the 3DP PEEK ribs were attached to the remaining rib using steel wires at one end. The steel wire was threaded through the side holes of the PEEK implant and wrapped around the remaining ribs. The other end was fixed to the sternum using 2 screws for internal fixation (Figure 2A). For patients with ribs defects in costal arch or spinal roots, 3DP PEEK implants of E type or vertical type were fixed with the remaining rib using steel wires (Figures 2B and 2C). For patients with whole sternum defects, 3DP PEEK whole sternum was bound with clavicle and residual ribs using steel wires (Figure 2D). For patients with partial sternal defect, 3DP PEEK sternum was anchored to the remaining sternum by using 8 screws in the proper places, and then it was fastened to the remaining ribs using steel wires (Figures 2E and 2F).

To repair the pleura, a pericardial patch (Guanhao Biotech Corporation, Guangzhou, China) was suspended on the inner surface of PEEK implants. The edge of the patch was sutured continuously with the remaining pleura. This approach may effectively reduce the dead space in the chest wall. The surgical incision was sutured directly in 43 patients with enough skin and muscle to cover the chest wall defect. Myocutaneous pedicled flaps, including the latissimus dorsi flap, pectoralis major myocutaneous flap and rectus abdominis musculocutaneous flap, were used to cover the larger soft tissue defects in 6 patients. A negative pressure drainage tube was retained between the 3DP implant and pericardial patch during surgery. All patients received an intravenous drip of ceftriaxone from a half hour before surgery until 72 h after surgery. Ultrasonography was performed to detect effusion in the chest wall. The drainage tube was removed when daily drainage was less than 30 mL.

QUANTIFICATION AND STATISTICAL ANALYSIS

Descriptive data are reported using the mean $\pm$ standard deviation. The Kaplan−Meier method was used to calculate OS and DFS probabilities. All recurrence and survival data were calculated from the date of surgical resection. Differences in OS and DFS were determined by log rank analysis. Some variables were used to evaluate the prognostic significance, including age, sex, tumor location, history of disease, histology, maximum tumor diameter (Dt), maximum tumor area (St), maximum defect diameter (Dd)/Dt (Figure 2G), maximum defect area (Sd)/St (Figure 2G), margin status, and neoadjuvant and adjuvant therapy. Significance was defined as $p < 0.05$. The data analysis was conducted using SPSS statistical package software (version 23.0; IBM SPSS Inc.).

ADDITIONAL RESOURCES

This work has been registered in Chinese Clinical Trial Registry (ChiCTR) Website, and the registration number is ChiCTR2300078408 and associated link is https://www.chictr.org.cn/bin/project/edit?pid=211860.