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ORIGINAL ARTICLE

Primary cardiac lymphoma: the management and outcome of a single-centre cohort of 22 patients

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ABSTRACT

Background: The incidence of primary cardiac lymphoma (PCL) is increasing, but the optimal management approach remains unclear. We assessed the clinical characteristics of a single-centre cohort with the goal of determining the optimal management approach. The treatment outcomes and prognostic factors are reported.

Material and methods: All PCL patients were diagnosed via biopsy guided by whole-body imaging (positron emission tomography/computed tomography [PET/CT] and/or contrast-enhanced CT]. Curative therapy involved either surgery or prephase steroids followed by definitive immunochemotherapy, depending on the histological type. The primary outcomes were overall survival (OS) and progression-free survival (PFS); the secondary outcome was the treatment response.

Results: Twenty-two PCL patients (14 males, 8 females; age: 59.5 ± 14.7 years [mean ± S.D.]) were histologically confirmed to have diffuse large B-cell lymphoma (DLBCL; $n = 17$ [77.3%]), fibrin-associated DLBCL (FA-DLBCL) ($n = 4$ [18.2%]) and Burkitt lymphoma ($n = 1$ [4.5%]). Seven patients underwent cardiotomy (three for biopsy, four with curative intent). The median and longest follow-up periods were 16.3 and 180.0 months, respectively. The 16 patients who received curative therapy (complete response [CR], $n = 15$ [93.8%]; partial response [PR], $n = 1$ [6.2%]) showed better survival than those who did not (5-year OS: 83.0 ± 11.3% vs. 0%; hazard ratio [HR]: 0.025[95% confidence interval, CI: 0.003–0.187], $p < 0.001$); 5-year PFS: 78.7 ± 11.0% vs. 0%, HR= 0.010[0.001–0.093], $p < 0.001$). The left ventricular ejection fractions (LVEF) before and after definitive treatment was 63.6 ± 2.4% and 64.6 ± 4.5%, respectively ($p = 0.275$, power = 0.318). Extrapericardial lesions were associated with poorer survival (5-year OS: 40.0 ± 29.7% vs. 100%, $p = 0.027$; 5-year PFS:40.0 ± 21.9% vs. 100%, $p = 0.010$).

Conclusions: Whole-body imaging is essential for diagnosis and prognosis. Curative therapy provided reasonable outcomes and survival; extrapericardial lesions were associated with a poorer treatment response.

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KEYWORDS
Primary cardiac lymphoma; PET/CT with contrast-enhanced CT; single-centre study; DLBCL: treatment outcomes

Background

Primary cardiac lymphoma (PCL) is rare and diffuse large B-cell lymphoma (DLBCL) is the predominant subtype [1,2]. Previously, PCL was primarily diagnosed post-mortem in immunocompromised patients; however, immunocompetent cases have been increasingly reported recently, probably because of advances in modern imaging and biopsy techniques [1,3–11]. The current understanding of PCL is based mainly on case reports, while the disease definition, clinical characteristics, optimal management, treatment outcomes, and prognostic factors remain unclear. Recently, Carras *et al.* reported a single-centre cohort study of 13 patients [12]. Despite the high rate of extracardiac involvement (9/13), cardiotomy was used for most (9/13) of the biopsies. However, cardiotomy may not be clinically feasible because it increases the risk of post-surgical complications and delays curative therapy. Given the increasing availability of advanced imaging and biopsy techniques, we believe that clinical management can be improved. Thus, we conducted a cohort study including 22 Asian PCL patients, and used a whole-body

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Supplemental data for this article can be accessed here.

imaging-guided diagnostic protocol to reduce the requirement for cardiotomy. The treatment outcomes and prognostic factors are reported below.

Material and methods

Study design and patients

This retrospective study was approved by our institutional review board and ethics committee. The need for written informed consent was waived, given the retrospective nature of the study. All data were anonymised in line with the Declaration of Helsinki and local regulations. The inclusion criteria were as follows: complete medical records and follow-up data; cardiac dysfunction or arrhythmia as the initial symptom; histologically confirmed lymphoma according to the World Health Organisation classification; and whole-body imaging to confirm that the tumour involved only the heart and/or pericardium (or that the intrapericardial mass was larger than, and distinct from, all extrapericardial masses combined in cases with extracardiac involvement). As there are no consensus criteria on how to differentiate PCLs from secondary cardiac lymphomas (systemic lymphomas involving the heart), we excluded patients with historical systemic lymphoma (or a history thereof), and those with significant B symptoms (fever, night sweats, and/or weight loss) on initial presentation. Data on 1,379 consecutive patients initially presenting with cardiac masses from 1 January 2005 to 31 October 2020 were retrieved, and 22 PCL patients were finally identified by a panel of imaging, pathology, oncology, haematology, and cardiology specialists using the criteria described above. Figure S1 shows the research flow.

Diagnostic workup

Whole-body imaging was performed to evaluate disease characteristics and determine the optimal biopsy route. Whole-body 18-fluorodeoxyglucose positron emission tomography/computed tomography (18 F-FDG PET/CT) combined with contrast-enhanced CT (CECT) was the imaging modality of choice, but for patients with limited economic resources whole-body CECT was also accepted (see Document S1 for a description of the imaging techniques). Bulky disease was defined as the largest dimension $\geq$7.5 cm of a cardiac tumour. If imaging revealed extracardiac involvement, biopsy was performed at the least invasive site. Peripheral lymph node or mass biopsy was the priority, followed by cytological investigation of pleural or pericardial effusion, and intrathoracic or intra-abdominal biopsy (mediastinoscopy or CT-guided fine needle aspiration biopsy [CT-FNAB]). For patients presenting with only intrapericardial lesions, we attempted transjugular endocardial biopsy, endobronchial ultrasonography-guided fine-needle aspiration biopsy (EBUS-FNAB), or video-assisted thoracic surgery (VATS), depending on the lesion location. Cardiotomy was the final option. All histological samples were reviewed by an experienced pathologist (F Z) as previously described [13].

Treatment and response evaluation protocol

For patients with cardiac fibrin-associated diffuse large B-cell lymphoma (FA-DLBCL), complete tumour resection (without prephase therapy or adjuvant post-surgical chemotherapy) was performed, as previously described [13]. For patients with cardiac DLBCL or Burkitt lymphoma, therapy was performed according to NCCN guidelines, with modifications applied as necessary by the oncologists in charge (XJ W & WY L), based on their experience and the individual patient status. Briefly, prephase prednisone (100 mg per day) was given to all patients for 7 days prior to the initiation of definitive immunochemotherapy, for the reasons previously described [14]. Anthracycline-based therapy with rituximab (CHOP-R) was the first line therapy for all DLBCL patients. Specifically, six cycles of full-dose CHOP-R chemotherapy were applied after one cycle of reduced-dose (50 $\sim$ 70%) CHOP therapy, to prevent cardiac perforation [15]. For patients with Burkitt lymphoma, the CODOX-M/IVAC-R protocol was used, with the treatment dose reduced to 70% for the first cycle. Notably, for extremely senile patients with poor Eastern Cooperative Oncology Group performance status (PS $\geq$3) and accompanying life-threatening diseases, the R2 protocol or a weekly R protocol was applied with palliative intent (Tables S1 and S2). Transthoracic echocardiography was performed before and after definitive immunochemotherapy to monitor treatment-related cardiac toxicity.

Treatment responses were evaluated after every two cycles of chemotherapy (e.g., after cycles 2, 4, 6, etc.) using previously described criteria [16,17], and were retrospectively reviewed by both oncology (XJ W and WY L) and imaging (H Y and SX W) specialists with reference to the Lugano classification. The objective response rate (ORR) considered both the complete response (CR) and partial response (PR). Salvage treatment was applied on clinical confirmation of stable or progressive disease (PD).

Surveillance protocol and survival endpoints

All patients were followed up every 3 months for the first 2 years, and at 6-monthly intervals thereafter up to 5 years. At each visit, a physical examination was performed and the serum lactate dehydrogenase (LDH) level was measured. Imaging was scheduled if indicated. Patients were censored on either their last follow-up visit or 30 November 2020. The overall survival (OS) was the time from diagnosis to death or censorship. The surrogate survival endpoint was progression-free survival (PFS); this period ended on disease progression, death, or censorship.

Statistical analysis

IBM SPSS Statistics (ver. 26.0; IBM Corp., Armonk, NY, USA) and R software (R Foundation for Statistical Computing, Vienna, Austria) were used for the analyses. Survival curves were plotted using the Kaplan–Meier method and compared with the log-rank test. The median survival was calculated

using the reverse Kaplan–Meier method. Hazard ratios (HRs) were calculated using the Weibull accelerated failure time model, as previously described [18]. Rates were compared using either the chi-squared or Fisher exact test, and mean values were compared with the two-sided paired *t*-test. *p*-Values <0.05 were deemed statistically significant. The Benjamini–Hochberg method was used to correct for multiple comparisons, as previously described [19]. Statistical power was calculated using the R packages statmod and powerSurvEpi [20,21].

Results

Patients

Initially, 26 patients were included, but 4 were subsequently excluded because of a history of cured DLBCL ($n=1$), coexisting systemic small lymphocytic lymphoma ($n=1$), or cardiac lesions abutting mediastinal lesions as revealed by imaging (peripheral T cell lymphoma and DLBCL, both $n=1$). Finally, 22 patients (14 males, 8 females; age: 59.5 ± 14.7 years [mean ± Standard deviation, S.D.]) were enrolled. Of note, most patients ($n=18$ [81.8%]) were diagnosed after January 2014; the incidence tended to increase with time (Figure S2). The median and longest time from clinical presentation to a confirmed diagnosis were 2.4 and 29 months, respectively. The cardiac manifestations were mainly cardiac dysfunctions and arrhythmias. Specifically, cardiac dysfunction (New York Heart Association [NYHA] Classification III ∼ IV) was evident in all patients; the most common symptoms reflected right-sided dysfunction and included dyspnoea (at rest or during exercise), fatigue, and ankle swelling. Arrhythmias were detected in 20 (90.9%) patients; atrioventricular block was the most common type ($n=11$, 50%). Notably, five of nine III atrioventricular block patients received permanent pacemakers. The histological evaluations, clinical presentations, therapeutic protocols, and treatment responses are listed in Table 1.

Imaging-based evaluation and biopsy

Eighteen (81.8%) patients underwent 18 F-FDG PET/CT and CECT, and 4 (18.2%) underwent whole-body CECT. Extrapericardial tumours were identified in eight (36.4%) patients. The details and biopsy routes are listed in Table 2. Notably, seven patients underwent cardiotomy because imaging revealed only intrapericardial involvement; the surgery was curative for patients with FA-DLBCL ($n=4$) but only diagnostic for patients with DLBCL ($n=3$).

Treatment and survival

The median and longest follow-ups were 16.3 and 180 months, respectively. The treatment responses and survival events are plotted in Figure 1. Three patients did not complete curative treatment (nos. 1, 12, and 24) and three received only palliative treatments (nos. 2, 18, and 22); all of these patients exhibited rapid disease progression (incomplete treatment: median OS:1.0 ± 0.7 months, median PFS: 0.4 ± 0.2 months; palliative treatment: median OS:5.0 ± 2.8 months, median PFS:1.5 ± 0.1 months, Figure S3), and were thus combined into one group receiving non-curative therapies for subsequent analysis.

Except for the four patients diagnosed with FA-DLBCL, all patients received prephase steroid therapy, and all exhibited rapid temporary improvement of cardiac symptoms and PS. Sixteen patients (DLBCL, $n=11$; FA-DLBCL, $n=4$; Burkitt lymphoma, $n=1$) received curative therapy, with a median follow-up period of 22 months (range: 3–180 months). During definitive immunochemotherapy, 15 patients (93.8%; DLBCL, $n=10$; FA-DLBCL, $n=4$; Burkitt lymphoma, $n=1$) achieved CR, whereas 1 (6.3%) DLBCL patient achieved PR but developed PD during follow-up. The ORR was thus 100%. The 5-year OS and PFS were significantly better than those of patients without curative treatment (5-year OS:83.0 ± 11.3 vs. 0%, HR:0.025 [95% confidence interval, CI: 0.003–0.187], $p<0.001$; 5-year PFS:78.7 ± 11.0 vs. 0%, HR: 0.010 [95% CI: 0.001–0.093], $p<0.001$) (Figure 2(A,B)).

Of the 16 patients who received curative therapy, 10 presented with only intrapericardial lesions (DLBCL, $n=6$; FA-DLBCL, $n=4$), and 6 with extrapericardial lesions (DLBCL, $n=5$; Burkitt lymphoma, $n=1$). Thus, we further analysed the treatment responses and survival of patients with DLBCL and FA-DLBCL receiving curative therapies. Despite the prevalence of well-recognised, unfavourable prognostic factors, patients without extrapericardial lesions exhibited excellent treatment responses and survival, regardless of the histological type, and were therefore combined into one group for subsequent survival analysis (Table 3). Compared to patients with extrapericardial lesions, patients without such lesions exhibited a slightly better treatment response (CR: 100 vs. 80.0%, $p=0.333$, power=0.25) but significantly better survival (5-year OS:100% vs. 40.0 ± 29.7%, $p=0.027$; 5-year PFS: 100% vs. 40.0 ± 21.9%, $p=0.010$) (Figure 2(C,D)).

Thus, we stratified the patients into three risk groups that differed significantly in terms of survival: (1) patients with only intrapericardial lesions (revealed by imaging) who received curative therapy (median OS and PFS not reached; 5 year OS: 100%; 5-year PFS: 100%); (2) patients with extrapericardial involvement who received curative therapy (5-year OS: 40.0 ± 29.7%; 5-year PFS: 40.0 ± 21.9%, median OS: 22.1 [95% CI: 0–48.8] months, median PFS: 13.5 [95% CI: 2.2–24.9] months) and (3) patients who did not receive curative therapy (5-year OS and PFS: 0%; median OS: 1.5 [95% CI: 0–6.3] months; median PFS: 1.4 [95% CI: 0.04–2.8] months) (Figure 2(E,F)).

Adverse effects and complications during treatment

Except for one patient (nos. 2, aged 87 years) who developed a rampant infection and died of septic shock, no severe complications were observed during treatment. Most patients developed only mild and clinically manageable side-effects, such as myelosuppression and pneumonia/pneumonitis. Transthoracic echocardiography-based surveillance revealed no significant decrease in left ventricular function (left

Table 1. Patient demographics.

Gender, *N*(%)	
Male	14 (63.6)
Female	8 (36.4)
Age/Years old, mean (S.D.)	59.5 (14.7)
PS $\geq$ 3[a], *N*(%)	15 (68.2)
LDH > 250IU/L, *N*(%)	20 (90.9)
IPI $\geq$ 3[b], *N*(%)	15 (68.2)
Time duration from presentation to diagnosis/ Months, median (range)	2.4 (0.7–29)
Bulky disease[c], N(%)	17 (77.3)
Histology, *N*(%)	
DLBCL	17 (77.3)
FA-DLBCL	4 (18.2)
Burkitt lymphoma	1 (4.5)
IHC of DLBCL, *N*(%)	
CD5+	8 (47.1)
BCL2 & c-Myc double-expressor	9 (52.9)
Ki67%$\geq$80%	12 (70.6)
Treatment regime[d], *N*(%)	
CHOP-R	12 (54.5)
CODOX-M/IVAC-R	1 (4.5)
Surgery	4 (18.2)
Palliative: R2	2 (9.1)
Palliative: Weekly R	1 (4.5)
Comfort care	2 (9.1)
Best treatment response, *N*(%)	
CR	15 (68.2)
PR	2 (9.1)
SD	4 (18.2)
PD	1 (4.5)
Cardiac arrhythmias, *N*(%)	
Atrioventricular block	11 (50.0)
I/II	2 (18.2)
III	9 (81.8)
Atrial fibrillation	2 (9.1)
Junctional escape rhythm	1 (4.5)
Incomplete right bundle branch block	2 (9.1)
Premature atrial contraction	2 (9.1)
Accelerated junctional rhythm	1 (4.5)
Sinus tachycardia	1 (4.5)
Normal	2 (9.1)
Cardiac dysfunction[e], *N*(%)	22 (100)
LVEF[f], before definitive treatment, mean (S.D.) %	63.6 (2.4)
LVEF[f], after definitive treatment, mean (S.D.) %	64.6 (4.5)

[a]Eastern Cooperative Oncology Group performance status.
[b]Burkitt lymphoma was not included.
[c]Bulky disease: $\geq$7.5 cm in the greatest dimension of an intracardiac mass.
[d]See Tables S1 and S2 for details of chemotherapies.
[e]Defined as the New York Heart Association [NYHA] Classification III$\sim$IV, mainly right-sided cardiac dysfunctions.
[f]By transthoracic echocardiography, for monitoring the treatment-related cardiac toxicity.
S.D.: standard deviation; PS: The Eastern Cooperative Oncology Group performance status; LDH: lactate dehydrogenase; IPI: international prognostic index; DLBCL: diffuse large B-cell lymphoma; FA-DLBCL: fibrin-associated diffuse large B-cell lymphoma; BCL2: B-cell lymphoma 2; c-Myc: cellular myelocytomatosis oncogene; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease (disease progression).

ventricular ejection fraction [LVEF] before and after definitive treatment: 63.6 ± 2.4 vs. 64.6 ± 4.5%, $p = 0.275$, power=0.318). Notably, no cardiac perforation was observed.

Discussion

This study described our experience with the largest single-centre PCL cohort reported to date. Whole-body imaging reduced the need for cardiotomy-biopsy compared to earlier reports [12]. Curative therapy was the most important prognostic factor; extracardiac involvement revealed by imaging was associated with poorer prognosis. Despite the presence of well-recognised unfavourable factors, the outcomes of curative treatments were reasonable in primary cardiac DLBCL patients, and better than previously described [1]. Moreover, we observed no significant cardiac toxicity, suggesting that the benefits of our regime outweigh the risks.

We found that the incidence of PCL tended to increase over time (Figure S2), in agreement with previous data [3]. However, we attributed this to advances in diagnostic and biopsy techniques, and improved understanding of the disease, rather than a real increase in prevalence. Although PCL is rare (<10%) among primary cardiac malignancies, the treatment outcomes are significantly better, emphasising the importance of timely diagnosis [1,3,22–24]. Cardiotomy is the most effective, but also the most invasive, diagnostic method, and is associated with a high likelihood of treatment refusal and thus diagnostic failure. Hence, we suggest the use of a whole-body imaging protocol to aid both diagnosis and biopsy, especially when extracardiac lesions are identified. Specifically, 8 of our 22 (36.4%) PCL patients exhibited extrapericardial lesions, and biopsy planning was facilitated by anatomical and metabolic information obtained with PET/CT with CECT (nos. 8, Figure S4). Six patients (27.3%) presented with large pericardial effusions, with or without pleural effusion, and were diagnosed cytologically. For patients showing only intrapericardial involvement, 18 F-FDG PET/CT combined with CECT revealed lesional masses within the heart, which informed the choice of an advanced biopsy technique such as intravascular endocardial biopsy (nos. 16, Figure S5), trans-bronchus FNAB (nos. 14, Figure S6), or VATS; only seven patients underwent cardiotomy. As PET/CT with CECT provides both anatomical and metabolic information, that combination is preferred to contrast-enhanced CT. Pulmonary embolisms (PEs) developed in two patients (nos. 16 and 10, Table S1) with right atrial tumour involvement, but resolved without further complications after early coadministration of anticoagulants, again emphasising the need for contrast-enhanced imaging [1].

Compared to a previous cohort (Carras 2017; see Table S3 for details), we performed significantly fewer cardiotomies (7/22 vs. 9/13, $p = 0.043$, power=0.490) despite encountering fewer cases with extrapericardial involvement (8/22 vs. 9/13, $p = 0.085$, power=0.39), probably because we performed whole-body imaging more frequently (22/22 vs. 4/13, $p < 0.001$, power=1.000), especially PET/CT (18/22 vs. 4/13, $p = 0.004$, power = 0.83) [12]. Interestingly, significantly more patients exhibited pericardial involvement in our cohort (12/22 vs. 0/13), probably because our diagnostic protocol places more emphasis on cytological and PET/CT evaluation.

Rapid tumour responses and improved cardiac function were observed in all PCL patients on prephase steroids; however, this has not been reported in patients with other common cardiac malignancies, such as sarcomas and metastases. Although cardiac inflammatory diseases, such as sarcoidosis and plasma cell granuloma, may present with similar characteristics, rapid alleviation of cardiac symptoms by a steroid may suggest the need for further invasive investigation, as the treatment outcomes of patients with both PCL and cardiac inflammatory diseases were reasonable [25–29].

Table 2. Imaging modalities, lesion locations, and biopsy routines.

Pre-treatment whole-body imaging evaluation, *N*(%)	
18F-FDG PET/CT with CECT	18 (81.8)
CECT	4 (18.2)
Tumour deposits identified by imaging modalities, *N*(%)	
Right atrium	13 (59.1)
Right ventricle	6 (27.3)
Left atrium	7 (31.8)
Left ventricle	1 (4.5)
Atrial septum	6 (27.3)
Ventricular septum	3 (13.6)
Pericardium	12 (54.5)
Cardiac vessels	6 (27.3)
Extrapericardium	8 (36.4)
Extra-pericardial lymph node	7 (87.5)
Adrenal gland	2 (25.0)
Bone	2 (25.0)
Pancreas	1 (12.5)
Intestine tract	1 (12.5)
Testicle	1 (12.5)
Muscle	1 (12.5)
Biopsy routes, *N*(%)	
Cardiotomy: curative intent	4 (18.2)
Cardiotomy: for biopsy	3 (13.6)
Lymph node biopsy	5 (22.7)
Cytology: pericardial effusion	4 (18.2)
Cytology: pleural effusion	2 (9.1)
VATS: pericardial biopsy	1 (4.5)
EBUS-FNAB: pericardial biopsy	1 (4.5)
Endomyocardial biopsy	1 (4.5)
CT-FNAB: adrenal gland	1 (4.5)

18 F-FDG: 18F-fluorodeoxyglucose; CT: computed tomography; PET: positron emission tomography; CECT: contrast-enhanced CT; EBUS: endobrounchus ultrasonography; FNAB: fine-needle aspiration biopsy. VATS: Video-assisted thoracoscopic surgery.

Bulky intrapericardial disease was evident in 17 of our 22 patients (77.3%), likely reflecting silent development and asymptomatic heart failure early in the disease course, along with the long period required for a final clinical diagnosis and the aggressive nature of PCL [1]. For such patients, rapid tumour debulking is necessary to stabilise the haemodynamics and improve cardiac function. Various surgeries have been proposed [30]; however, our treatment achieved similar effects within days, so we hypothesise that tumour debulking *via* chemotherapy is adequately rapid; surgery may not be necessary for most patients. On the other hand, bulky DLBCL is a risk factor for residual disease and further radiation may be necessary [31]. However, all of our bulky cardiac DLBCL patients showed good survival and none required further radiation. Thus, cardiac DLBCL may differ from other DLBCLs.

We found that extrapericardial lesions revealed by imaging correlated with poorer OS and PFS, as reported previously [1]. However, the survival of DLBCL patients without extrapericardial lesions was excellent, as was that of patients with FA-DLBCL, despite a high proportion of well-recognised unfavourable factors such as c-Myc and BCL-2 double expression, CD5+ status, a high LDH level, an International Prognostic Index (IPI) $\geq$3, and bulky disease. Although our sample size was small, our data suggest that extrapericardial involvement is very important in terms of prognosis.

Although our PCL cohort is clearly the largest described to date, the sample size of this study was nevertheless relatively small, and our results should be further validated.

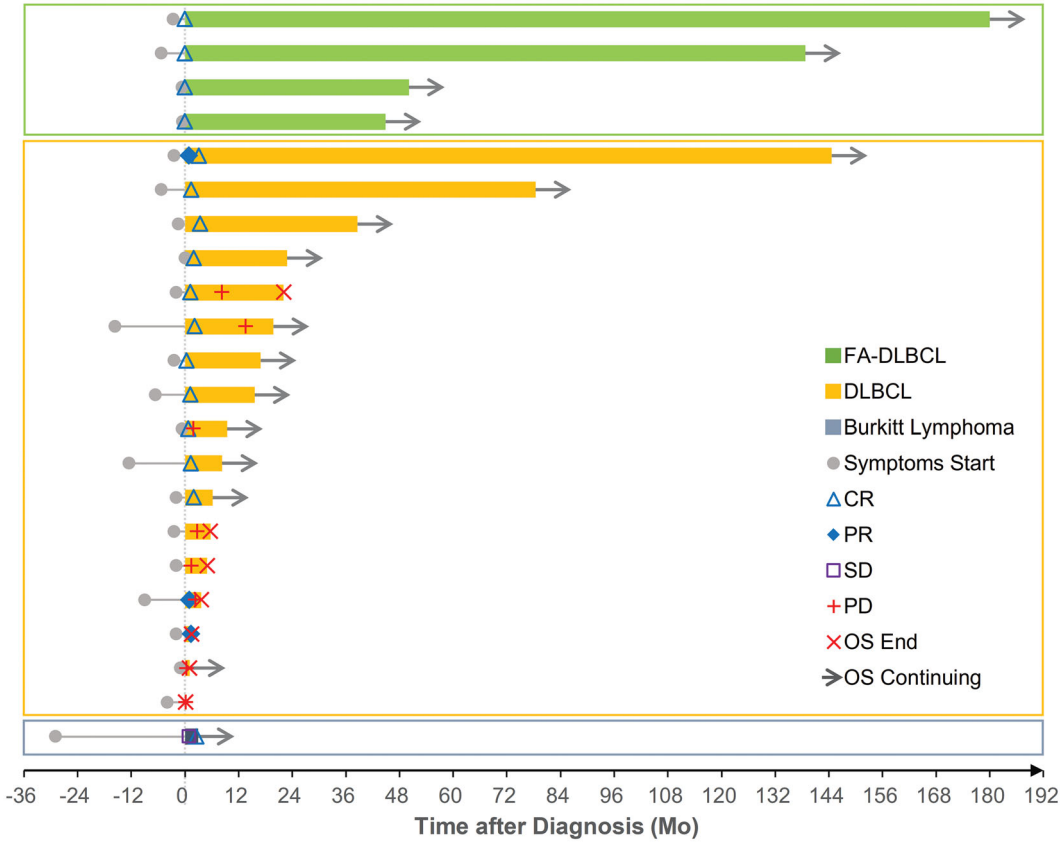

Figure 1. Swimmer plot of all patients, showing the treatment responses and survival status. DLBCL: diffuse large B-cell lymphoma; FA-DLBCL: fibrin-associated diffuse large B-cell lymphoma; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; OS: overall survival; Mo: months.

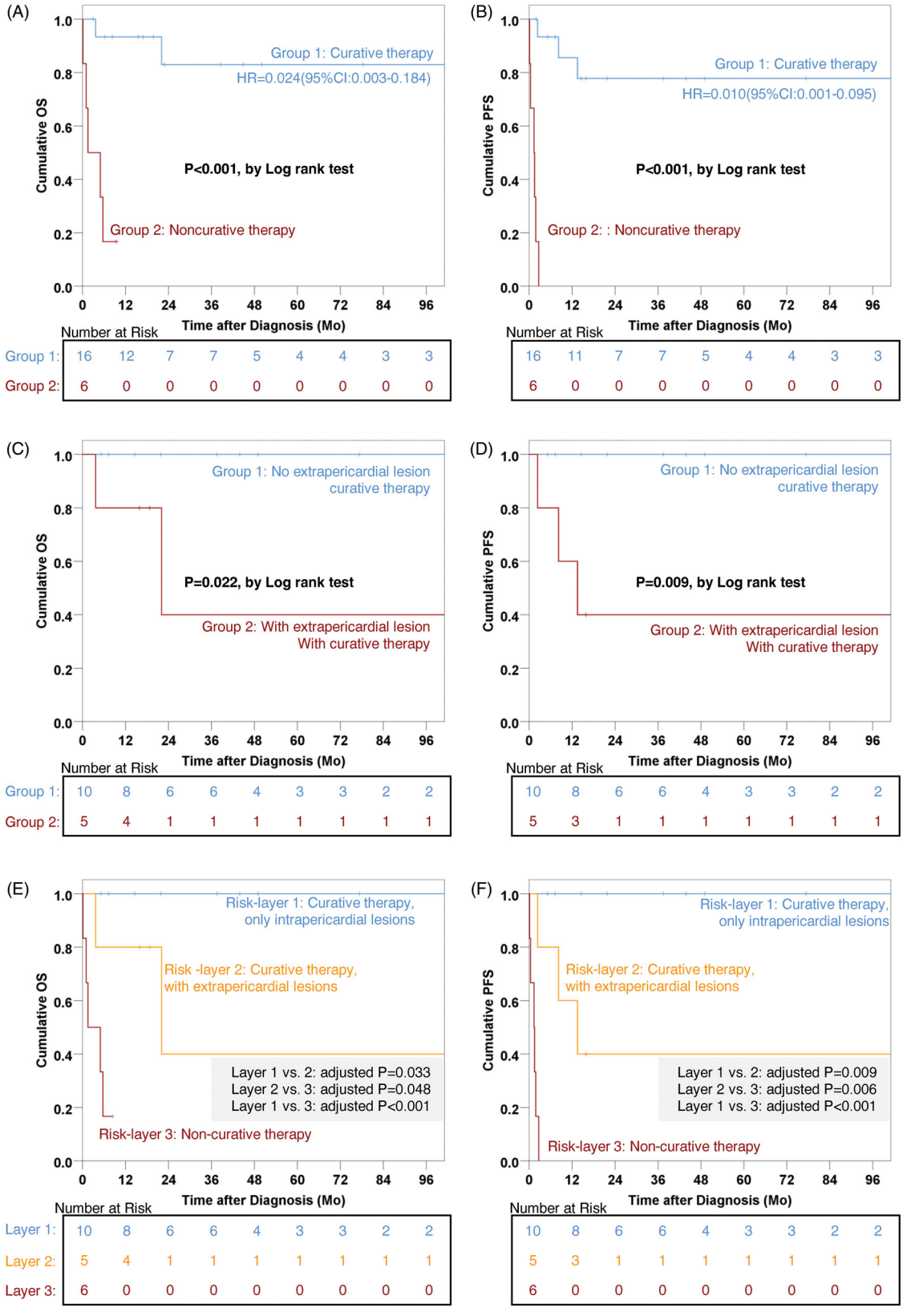

Figure 2. Survival curves of the different groups. (A and B) Patients who received (blue line) and did not receive (red line) curative therapy, respectively, using OS (A) and PFS (B) as the endpoints. (C and D) Patients without and with extrapericardial lesions (blue and red lines, respectively) using OS (C) and PFS (D) as the endpoints. (E and F) Patients with different risk levels, as follows: risk level 1 (blue line): patients with only intrapericardial lesions who received curative therapy; risk level 2 (yellow line): patients with extrapericardial involvement who received curative therapy; and risk level 3 (red line): patients who did not receive curative therapy. In all cases, OS (E) and PFS (F) were the endpoints. In C–F, the patient with Burkitt lymphoma was excluded because of histological differences and the sample size of only 1 case. OS: overall survival; PFS: progression-free survival; Mo: months; DLBCL: diffuse large B cell lymphoma.

Table 3. Clinical characteristics of patients with curative therapy: FA-DLBCL vs. DLBCL.

	FA-DLBCL	DLBCL	
	No extrapericardial lesion	No extrapericardial lesion	With extrapericardial lesion
	$N = 4$	$N = 6$	$N = 5$
CD5+, (*n/N*)	3/4	2/6	3/5
Ki67 > 80%,(*n/N*)	3/4	5/6	3/5
BCL2 & c-Myc double-expressor, (*n/N*)	1/4	4/6	2/5
LD*H* > 250IU/L, (*n/N*)	4/4	5/6	5/5
IP*I* ≥ 3, (*n/N*)	4/4	4/6	5/5
Bulky disease[a], (*n/N*)	3/4	6/6	5/5
CR, (*n/N*)	4/4	6/6	4/5
5-Year OS, rate (S.D.)%	100 (/)	100 (/)	40.0(29.7)
5-Year PFS, rate (S.D.)%	100 (/)	100 (/)	40.0(21.9)

[a]Bulky disease: ≥7.5 cm in the greatest dimension of an intracardiac mass.
FA-DLBCL: fibrin-associated diffuse large B-cell lymphoma; DLBCL: diffuse large B-cell lymphoma; BCL2: B-cell lymphoma 2; LDH: lactate dehydrogenase; IPI: international prognostic index; CR: complete response; OS: overall survival; PFS: progression-free survival.

Nevertheless, the data highlight the importance of whole-body imaging, especially PET/CT combined with contrast-enhanced CT, for diagnosis and prognosis. Moreover, despite some difficulties in diagnosis, the outcomes of curative therapy were reasonable. Efforts should be made to achieve earlier diagnosis and thus improve survival.

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Author contributions

XJ Wei & H Yuan: contributed to the conceptualisation, methodology, investigation, data curation, formal analysis, verification, Writing–original draft, Writing–review& editing, and visualisation. PL Khong: methodology, Writing–review& editing. F Zhang, PJ Liao, XM Jiang, L Huang, HG Guo, FL Chen, SC Liu &YY Huang: resources, investigation, Writing–review & editing. SX Wang: Certified statistician, methodology, formal analysis, verification, and supervision. WY Li: Conceptualisation, methodology, investigation, validation, writing–review & editing, visualisation, supervision, and project administration.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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