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The natural history and surgical outcome of patients with scimitar syndrome: a multi-centre European study

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Aims Treatment decisions in patients with scimitar syndrome (SS) are often challenging, especially in patients with isolated SS who are often asymptomatic and who might be diagnosed accidentally. We queried a large multi-institutional registry of SS patients to evaluate the natural history of this condition and to determine the efficacy of surgical treatment in terms of survival and clinical status.

Methods and results We collected data on 485 SS patients from 51 institutions; 279 (57%) patients were treated surgically (STPs) and 206 (43%) were clinically monitored (CMPs). Median age at last follow-up was 11.6 years (interquartile range 4–22 years). Overall survival probability at 30 years of age was 88% [85–92% confidence intervals (CI)] and was lower in patients with associated congenital heart disease (CHD) ($P < 0.001$) and pulmonary hypertension ($P < 0.001$). Most patients were asymptomatic at last follow-up (279/451, 62%); STPs were more frequently asymptomatic than CMPs (73% vs. 47%, $P < 0.001$), with fewer cardiac [odds ratio (OR) 0.42, 95% CI 0.22–0.82] and respiratory symptoms (OR 0.08, 95% CI 0.02–0.28). Many STPs (63/254, 25%) had stenosis/occlusion of the scimitar drainage, and this was associated with a younger age at surgery (OR 0.4, CI 0.21–0.78).

Conclusion Patients with SS have a high overall survival. Survival probability was lower in patients with associated CHDs and in patients with pulmonary hypertension. Surgical treatment of SS is beneficial in reducing symptoms, however, given the significant risk of post-operative scimitar drainage stenosis/occlusion, it should be tailored to a comprehensive haemodynamic evaluation and to the patient's age.

Keywords Congenital heart defect • Surgery • Natural history • Multi-centre study

Introduction

Scimitar syndrome (SS) is a rare congenital heart defect (CHD) characterized by anomalous venous drainage of part or the entire right lung to the inferior vena cava, variable right lung hypoplasia, and variable systemic blood supply to part of the right lung.[1–3] Symptoms vary dramatically and are difficult to ascribe to the anomalous pulmonary vein drainage, to the presence of associated cardiac anomalies or to a combination of both.[4–11] Most patients present with symptoms during early infancy and need prompt surgical intervention.[2,6,7] Treatment decisions are often challenging in patients with isolated SS (i.e. without associated CHDs) who are often incidentally diagnosed during adolescence or adulthood and they usually remain asymptomatic or mildly symptomatic for many years and are able to lead a normal life.[1,2,8,9,12]

To address this issue, and with the aim of improving patient care and clinical practice, we used a large multi-institutional registry of patients

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† See Appendix 1. On the behalf of the European Congenital Heart Surgeon Association (ECHSA) and European Association for Paediatric Cardiology (AEPC).

with SS to analyse the natural history of the condition, and the efficacy of surgical treatment in terms of survival and clinical status. To our knowledge, this is the largest series of SS patients reported thus far.

Methods

The Clinical Investigation Committee of the University Hospital of Padua approved the retrospective review of medical records in accordance with the protection of patient confidentiality. Patients were not identified and individual consent was not required (protocol no. 18946/2016). Fifty-one institutions contributed to data collection, including 40 European and 11 extra-European institutions. The study was conducted on the behalf of the Association for European Pediatric Cardiology (AEPC) and of the European Congenital Heart Surgeons Association (ECHSA). We included data from any patient with SS who was treated surgically (STPs) or clinically monitored (CMPs). Patients with SS who underwent repair of associated CHDs without correction of the anomalous pulmonary venous connection ($n = 20$) were considered CMPs. We excluded patients with a functional single ventricle ($n = 18$) because their outcome could be influenced by their specific physiology. Demographic, clinical, morphological, and operative data were collected. Other associated CHDs were divided arbitrarily into simple CHDs (including atrial septal defects and/or patent ductus arteriosus) and complex CHDs (including all other CHDs). We defined pulmonary arterial hypertension as a the presence of a mean pulmonary artery pressure above 25 mmHg at rest or 50% above systemic level, either by direct measurement in a catheterization laboratory or by two-dimensional echocardiography estimation using tricuspid regurgitation Doppler velocity.[13,14] We arbitrarily divided patients into three groups according to their age at diagnosis: (i) neonates/infants (≤1 year), (ii) children (between 1 and 10 years), and (iii) adolescents/adults (>10 years).

Outcomes

Primary outcomes were to evaluate the natural history of this condition and to determine the efficacy of surgical treatment in terms of survival and clinical status (defined as the presence and type of symptoms at the last clinical evaluation).

Statistical analysis

Continuous variables are expressed as median, with interquartile range (IQR) and categorical variables as percentages (absolute numbers). Univariate comparisons for nominal variables were performed with the χ^2 test or the omnibus F test for continuous variables. No *post hoc* analysis was performed. The relationship between continuous and nominal variables was assessed with the Mann–Whitney test. For multi-variable analysis, we used linear regression and logistic regression for continuous and dichotomic variables, respectively. Survival curves were calculated with the Kaplan–Meier method, and difference in survival probability by the log-rank test.

To determine the efficacy of surgical treatment, we compared the outcome of STPs with that of CMPs. Associations among clinical variables and outcome measures were based on a logistic regression model for binary outcomes and expressed as odds ratios (OR) or using a Cox proportional hazard model, and expressed as hazard ratios (HR) with a 95% confidence interval (CI). In case of multiple regressors, fit in both models was evaluated using the Akaike information criterion and selected the model with the lower value. Cross-validation and bootstrap (5000 runs) techniques were applied to assess the fitting accuracy of the models. Somer's concordance index Dxy (the closer to 1 in absolute value the better) was obtained to evaluate goodness of fit and adjusted for optimism. To evaluate the efficacy of surgery, we built a propensity score model[15] to adjust for selection bias of patients selected for surgery, both considering the overall population and patients with isolated SS. The selection model was based on all baseline clinical variables (gender, age at diagnosis, cardiac symptoms at diagnosis, respiratory symptoms at diagnosis, heart position, dilated right ventricle at diagnosis, associated CHDs, systemic arterial supply (SAS) to the right lung, pulmonary hypertension, and right pulmonary hypoplasia) and implemented using a genetic algorithm.[16] Patients were matched according to the propensity score on a 1:1 basis. Bias-adjusted ORs and HRs were obtained[17] by adjusting for propensity score and clustering by matched pairs using a Huber–White estimator.[18] Statistical significance was set at $P < 0.05$ (two-sided). *P*-values are reported with Benjamini & Yekutieli correction for multiplicity.[19] For the analysis we used R-software,[20] the Matching,[21] Harrell's rms[22] package, and the alluvial package by Bojanowski and Edwards.[23]

Results

Patient population

We collected data on 485 patients from 51 institutions (*Figure 1*). Each centre provided the data of a median of six patients (IQR 2–11). Median age at diagnosis was 0.48 years (IQR 0.1–5.2 years). Most

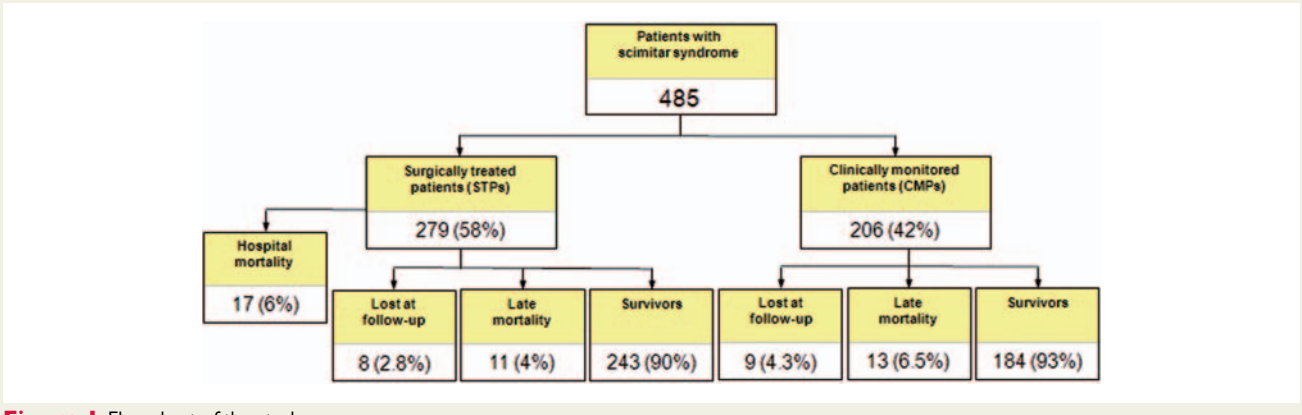

Figure 1 Flowchart of the study.

patients were women ($n = 305$, 63%). Diagnosis of SS was established by two-dimensional echocardiography. Additional investigations were: cardiac catheterization ($n = 276$, 57%), chest computed tomography scan ($n = 146$, 30%), cardiac MRI ($n = 72$, 15%), and lung scintigraphy ($n = 74$, 15%). The propensity score model built to limit the selection bias, used in the next sections, performed satisfactorily in classifying STPs vs. CMPs (Dxy 0.48, after considering optimism with 10 000 bootstrap replications).

Anatomy

The anomalous right pulmonary venous drainage involved the inferior lobe in 136 patients (28%), the inferior and middle lobes in 54 (11%) and the entire right lung in 278 (57%). Less frequent drainage patterns were present in the remaining 17 patients (4%). Three hundred and forty-six patients (71%) presented with some degree of right lung hypoplasia (*Table 1*). The severity of right lung hypoplasia correlated with age at diagnosis (the younger the patient, the more

Table 1 Demographic, clinical/instrumental data and outcomes according to the age of patients at diagnosis

	Overall	Age groups (at diagnosis)			
		Neonates/infants (0–1 year)	Children (≥1–10 years)	Adolescents/adults (≥10 years)	*P*-value corrected for multiplicity
Number of patients[a]	485 (100%)	*n* = 282 (58%)	*n* = 113 (23%)	*n* = 90 (19%)	
Gender, female[a]	305 (63%)	166 (59%)	70 (63%)	69 (77%)	0.03
Heart position					
Dextrocardia[a]	240 (49%)	148 (52%)	61 (54%)	31 (34%)	0.05
Mesocardia[a]	83 (17%)	48 (17%)	19 (17%)	16 (18%)	
Levocardia[a]	163 (33%)	86 (30%)	33 (29%)	43 (48%)	
Isolated forms[a]	186 (38%)	81 (29%)	57 (50%)	48 (53%)	0.003
Associated CHD[a]	299 (62%)	199 (71%)	60 (53%)	40 (44%)	0.003
Simple CHDs[a]	198 (41%)	116 (41%)	49 (43%)	33 (37%)	
Complex CHDs[a]	101 (21%)	83 (29%)	11 (9.7%)	7 (7.8%)	
Atrial septal defect	243 (50%)	156 (55%)	56 (46%)	35 (39%)	0.01
Right pulmonary hypoplasia[a]	346 (71%)	220 (78%)	76 (67%)	50 (55%)	0.003
Degree of RPH					
Mild[a]	204 (59%)	115 (52%)	50 (66%)	39 (78%)	0.003
Moderate[a]	96 (28%)	65 (30%)	21 (28%)	10 (20%)	
Severe[a]	46 (13%)	40 (18%)	5 (6%)	1 (2%)	
Symptoms at diagnosis[a]	353 (73%)	220 (78%)	73 (65%)	60 (67%)	0.047
Cardiac symptoms[a]	227 (47%)	168 (60%)	29 (27%)	30 (33%)	0.006
Respiratory symptoms[a]	243 (50%)	140 (50%)	59 (52%)	44 (49%)	0.99
Dilated RV at diagnosis (at 2D-echo)[a]	332 (68%)	186 (66%)	84 (74%)	62 (69%)	0.99
Cardiac catheterization[a]	276 (57%)	154 (55%)	75 (66%)	47 (52%)	0.24
Qp:Qs[b]	2.1:1 (1.5:1–2.6:1)	2:1 (1.4:1–2.7:1)	1.8:1 (1.5:1–2.3:1)	2:1 (1.6:1–2.2:1)	0.99
mPAP (mmHg)[b]	24 (18–34)	26 (20–40)	20.5 (17–30)	24 (18.5–28)	0.006
Pulmonary hypertension[a]	157 (32%)	112 (40%)	28 (25%)	17 (19%)	0.006
SAS to the right lung[a]	248 (51%)	182 (65%)	49 (43%)	17 (19%)	0.006
Embolization of SAS[a]	177 (71%)	132 (47%)	33 (29%)	12 (13%)	0.006
STPs[a]	279 (58%)	142 (51%)	78 (69%)	59 (66%)	0.03
CMPs[a]	206 (42%)	140 (49%)	35 (31%)	31 (34%)	—
Time to last follow-up (years)[b]	7.2 (2.2–14)	6.4 (1.8–12.7)	9.9 (3.7–17)	7.5 (2.3–12)	0.02
Overall mortality[a]	41 (8.7%)	37 (13%)	4 (3.5%)	—	0.01
STPs hospital mortality[a]	17 (6%)	14 (9.8%)	3 (3.8%)	—	0.08
STPs late mortality[a]	11 (3.9%)	10 (7%)	1 (1.3%)	—	0.08
CMPs mortality[a]	13 (6.3%)	13 (9.3%)	—	—	0.14
Symptoms at follow-up[a]	172/451 (37%)	109 (42%)	33 (31%)	30 (35%)	0.24
Cardiac symptoms[a]	227 (47%)	168 (60%)	29 (27%)	30 (33%)	0.01
Respiratory symptoms[a]	243 (50%)	140 (50%)	59 (52%)	44 (49%)	0.99

ASA, systemic arterial supply; CHD, congenital heart disease; CMPs, clinically monitored patients; Qp, Qs, pulmonary-systemic blood flow ratio; mPAP, mean pulmonary artery pressure; RV, right ventricle, STPs, surgically treated patients; 2D, two-dimensional.
[a]Number of patients and percentage.
[b]Median and interquartile range.

severe the right lung hypoplasia, OR 0.88, 95% CI 0.81–0.96) and with the presence of symptoms (OR 1.48, 95% CI 1.24–1.76). Other associated CHDs were present in 299 patients (62%) (see Supplementary material online, *Table S1*): simple CHDs in 198 (41%) and complex CHDs in 101 (21%) patients. Atrial septal defect ostium secundum type was the most common associated CHD ($n = 243$ patients, 50%). The remaining 186 patients (38%) had isolated SS (see Supplementary material online, *Table S2*). An anomalous SAS to the right lung was demonstrated in 248 patients (51%) and its occlusion was deemed necessary in 177 patients (36%). A total of 332 patients (68%) had moderate/severe dilatation of the right ventricle.

Clinical presentation

Most patients were diagnosed in the neonatal/infant period ($n = 282$, 58%), 113 (23%) during childhood, and 90 (19%) in adolescence or adulthood. Three hundred and fifty-three patients (73%) were symptomatic upon diagnosis: respiratory symptoms (including respiratory distress, recurrent upper respiratory tract infections, cyanosis, and pneumonia) occurred in 243 patients (50%) and cardiac symptoms (including failure to thrive and congestive heart failure) in 227 patients (47%) (117 patients had mixed cardiac and respiratory symptoms). The remaining 132 patients (27%) were asymptomatic at diagnosis (65 patients having isolated SS). Neonates/infants were more frequently symptomatic at diagnosis ($P = 0.047$) than patients in the other two age-groups, and symptoms were mainly of cardiac origin ($P = 0.02$). At univariate analysis, cardiac symptoms were correlated to the presence of collateral arteries supplying the right lung ($P = 0.03$) and to right ventricular dilatation ($P = 0.01$). All these variables were statistically significant also at multi-variable analysis.

Physiology

One hundred and fifty-seven patients (32%) had pulmonary arterial hypertension, which was mostly seen in neonates/infants but was also found in children and in adolescents/adults. This condition was more frequent in patients with other associated CHDs (128/299 patients, 43%) than in patients with isolated SS (29/186 patients, 16%, $P = 0.01$). The median pulmonary to systemic blood flow ratio (Qp:Qs) was 2:1 (IQR 1.5:1–2.6:1). Univariate analysis revealed a correlation between Qp:Qs and associated CHDs ($P = 0.006$), cardiac symptoms ($P = 0.02$), and pulmonary hypertension ($P = 0.01$). At multi-variable analysis only pulmonary hypertension was statistically significant, which suggests a correlation among the explanatory variables.

Early outcome of surgically treated patients (hospital outcome)

Two hundred and seventy-nine patients (57%) were treated surgically (*Figure 1*). Median age at surgery was 4.2 years (IQR 0.5–12.6 years); symptomatic patients were treated earlier (median age of 2.3 years, IQR 0.4–10.7 years) especially in case of cardiac symptoms (median age of 0.8 years, IQR 0.3–6.7 years). Surgically treated patients more frequently had cardiac symptoms at diagnosis (147/279, 53%) than did CMPs (80/206, 39%, $P = 0.003$) (see Supplementary material online, *Table S3*). Two hundred and fifty-four patients (92%) underwent correction of the anomalous venous drainage, and 25 (8%) underwent right lung resection, namely, right lung lobectomy (n 18) and right lung pneumectomy ($n = 7$). Patients who underwent right pneumectomy/lobectomy were diagnosed earlier (median age at diagnosis was 1 months, IQR 0.3–8 months vs. 12 months, IQR 1–90 months, $P < 0.001$), presented more frequently cardiac symptoms

Table 2 Variables associated with mortality

	Deaths	Survivors	
Hospital mortality (STPs)	***n* = 17 (6%)**	***n* = 262 (94%)**	**OR (95% CI)**
Age at surgery (years)[a]	0.16 (0.08–0.3)	5 (0.7–15)	0.11 (0.01–0.79)
Associated CHDs[b]	16/17 (94%)	178/262 (68%)	2.23 (0.79–6.26)
Complex CHDs[b]	8/17 (47%)	55/262 (21%)	12.21 (1.48–100.42)
Pulmonary hypertension[b]	12/17 (71%)	93/262 (36%)	2.33 (1.05–5.16)
Cardiac symptoms[b]	17/17 (100%)	130/262 (49%)	24.6 (3.31–183.6)
Follow-up mortality (STPs)	***n* = 11 (4.3%)**	***n* = 243 (95.7%)**	**HR (95% CI)**
Age at surgery (years)[a]	0.2 (0.6–2.3)	14 (7–24)	0.07 (0.01–0.42)
Associated CHDs[b]	11/11 (100%)	161/243 (66%)	2.99 (1.40–6.40)
Complex CHDs[b]	7/11 (64%)	44/243 (18%)	25.51 (3.36–193.3)
Pulmonary hypertension[b]	10/11 (91%)	83/243 (34%)	3.31 (1.72–6.38)
Cardiac symptoms[b]	10/11 (91%)	117/43 (48%)	17.8 (4.28–73.68)
Natural history mortality (CMPs)	***n* = 13 (6.6%)**	***n* = 184 (93.4%)**	**HR (95% CI)**
Associated CHDs[b]	11/13 (85%)	86/184 (47%)	2.99 (0.87–10.23)
Complex CHDs[b]	7/13 (54%)	30/184 (16%)	11.23 (2.33–54.15)
Pulmonary hypertension[b]	8/13 (62%)	42/184 (23%)	7.02 (2.11–23.35)
Cardiac symptoms[b]	12/13 (92%)	64/184 (35%)	2.61 (1.14–6.01)

OR, odds ratio; HR, hazard ratio; CI, confidence interval; CHDs, congenital heart diseases; STPs, surgically treated patients.
[a]Median and interquartile range percentile.
[b]Number of patients and percentage: *n* (%).

(18/25, 72%, vs. 129/254, 51%, $P = 0.05$) and had more frequently a moderate/severe degree of right lung hypoplasia (11/17, 64% vs. 68/254, 39%, $P = 0.01$) then patients who underwent corrective surgery.

Corrective procedures were re-routing the scimitar vein into the left atrium ($n = 176$ patients) and direct 'scimitar vein re-implantation' into the left atrium ($n = 78$ patients). Associated CHDs were repaired during surgery. Ninety-three patients (33%) had postoperative complications, which were more frequent in neonates/infants (65/142, 46%) than in children (18/78, 23%) or in adolescents/adults (10/19, 17%; $P = 0.01$). Seventeen patients (6%) died in hospital (*Figure 1*, *Table 1*). Hospital mortality was lower for patients who underwent corrective surgery than for patients who underwent right lung resection (8/254, 3.1% vs. 9/25, 36%, $P = 0.01$) (see Supplementary material online, *Table S4*). Variables associated with hospital mortality are listed in *Table 2*.

Follow-up outcomes

Follow-up data were available for 451/468 (96%) patients. Median age at last clinical/instrumental evaluation was 11.6 years (IQR 4–22 years, maximum 78 years) and it was higher in STPs (14 years, IQR 6.5–24 years) than in CMPs (8 years, IQR 2.4–18 years; $P < 0.001$). Twenty-four patients died during follow-up, 11/254 STPs (4.3%) all after corrective surgery, and 13/197 CMPs (6.6%) (see Supplementary material online, *Table S4*). Variables associated with mortality are listed in *Table 2*. Overall survival probability at 30 years of age was 88% (CI 85–92%) was lower in patients with associated CHDs ($P < 0.001$) and in patients with pulmonary hypertension ($P < 0.001$) (*Figure 2*). The presence of pulmonary hypertension was associated with a lower survival, both in patients with isolated SS than in patients with associated CHDs (*Figure 2*).

The majority patients were asymptomatic at the last clinical examination (279/451, 62%) (*Figure 3*) and symptoms were fewer in STPs than in CMPs (OR 0.16, CI 0.08–0.32); this applies to both cardiac (OR 0.42, CI 0.22–0.82) and respiratory symptoms (OR 0.12, CI 0.05–0.28). Also considering patients with isolated SS only ($n = 186/485$), both cardiac (OR 0.20, CI 0.04–0.95) and respiratory symptoms (OR 0.08, CI 0.02–0.28) were fewer at follow-up in STPs than in CMPs.

Coil embolization of anomalous SAS to the right lung was associated with a reduction of cardiac symptoms between diagnosis and the last clinical examination in CMPs (OR 3.72, CI 1.48–9.35). Variables associated with last clinical status are listed in *Table 3*.

No patient who was asymptomatic at diagnosis developed symptoms after surgical treatment (0/65, 0%), whereas 6/60 (10%) of asymptomatic CMPs developed symptoms at the last clinical examination ($P = 0.01$): cardiac symptoms in three patients and respiratory symptoms in three others.

Late surgical complications in surgically treated patients

Sixty-three patients (25%) had an instrumental diagnosis of stenosis/occlusion of the scimitar drainage after a corrective procedure. This diagnosis was unrelated to the type of corrective technique used and it was more frequent in neonates/infants ($n = 40/12$, 33%) than in either children ($n = 15/75$, 20%) or adolescents/adults ($n = 8/57$, 14%; $P = 0.01$). There was an inverse linear correlation between age at

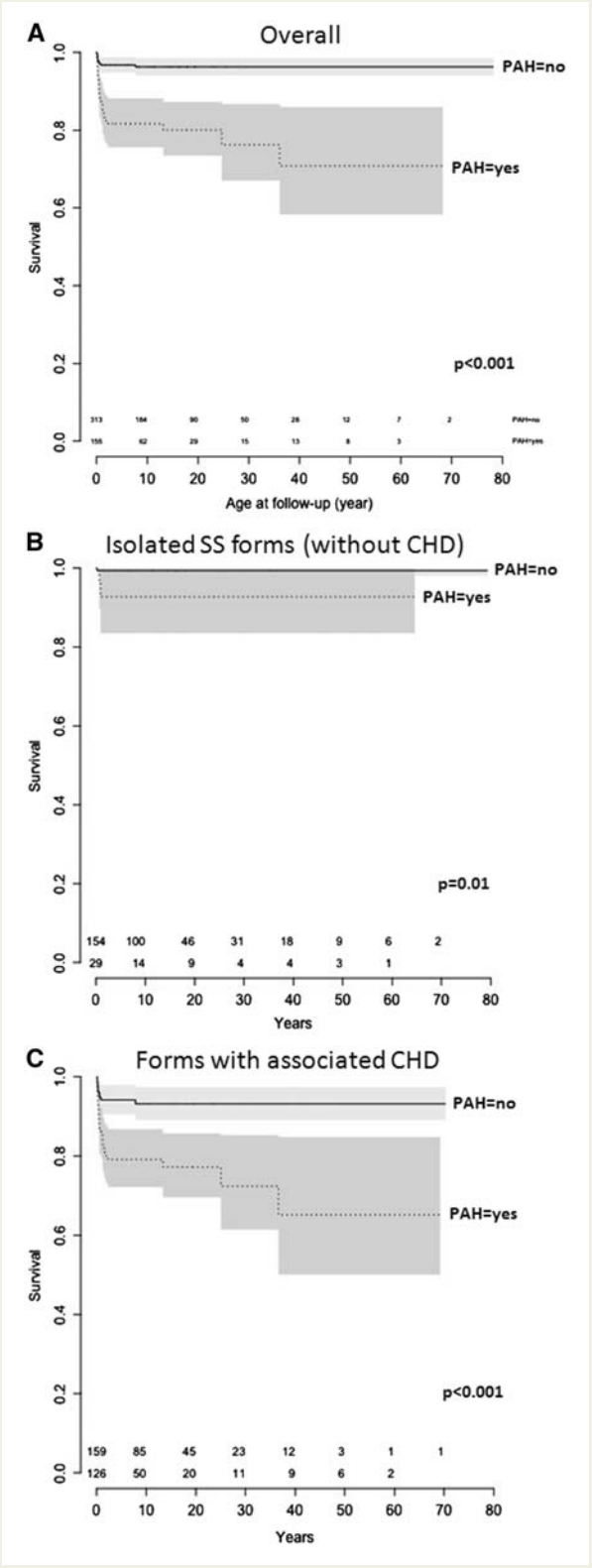

Figure 2 Survival probability according to Kaplan–Meier (age of patients at last follow-up examination with 95% confidence bands) of patients with pulmonary hypertension: (*A*) overall population and stratified by (*B*) patients with isolated SS (without congenital heart diseases, CHDs) and (*C*) patients with associated CHDs. SS, scimitar syndrome.

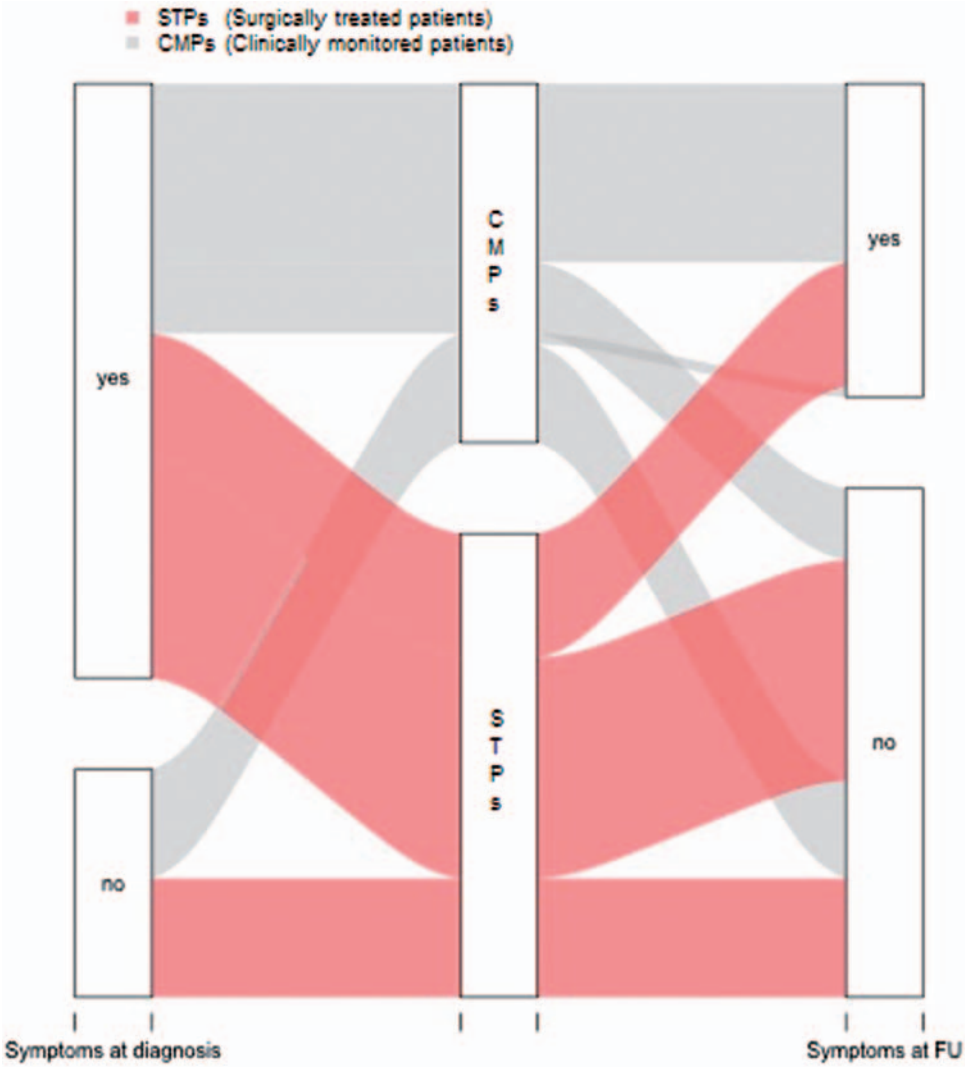

Figure 3 Flowchart showing the variation of patient's clinical status between the diagnosis and last follow-up examination (stratified by natural history vs. surgical treatment).

Table 3 Variables associated with late clinical outcome (symptomatic vs. asymptomatic patients)

	Symptomatic points *n* = 172 (38%)	Asymptomatic points *n* = 279 (62%)	
STPs (*n* = 254)	***n* = 68 (27%)**	***n* = 186 (73%)**	**HR (95% CI)**
Associated CHDs[a]	54/68 (79%)	118/186 (63%)	1.45 (0.73–2.9)
Complex CHDs[a]	19/68 (28%)	32/186 (17%)	1.80 (1.07–3.02)
Pulmonary hypertension[a]	35/68 (51%)	58/186 (31%)	2.02 (1.18–3.46)
Cardiac symptoms[a]	53/68 (78%)	74/186 (40%)	5.81 (3.14–10.77)
CMPs (*n* = 197)	***n* = 104 (53%)**	***n* = 93 (47%)**	**HR (95% CI)**
Pulmonary hypertension[a]	38/104 (37%)	12/93 (13%)	5.16 (2.32–11.47)
Cardiac symptoms[a]	60/104 (58%)	16/93 (17%)	8.40 (4.06–17.36)

STPs, surgically treated patients; CMPs, clinically monitored patients; OR, odds ratio; HR, hazard ratio; CI, confidence interval; CHDs, congenital heart diseases.
[a]Number of patients and percentage: *n* (%).

correction and stenosis/occlusion of the scimitar drainage (the younger the patient, the higher incidence of stenosis/occlusion) (OR 0.4, CI 0.21–0.78). Forty-two of these 63 patients (67%) underwent re-operation or haemodynamic intervention at a median of 0.8 years (IQR 0.5–1.2 years) after repair. The outcome of patients with postoperative scimitar vein stenosis/occlusion is shown in *Figure 4*.

Discussion

The clinical presentation of patients with SS is extremely variable. Symptomatic patients with SS, especially in case of cardiac symptoms, usually need prompt surgical intervention;[2,24] this consists of redirection of the anomalous pulmonary venous drainage into the left atrium.[25–27] Right lung lobectomy or pneumonectomy may be required in patients with severe clinical features.[2,28,29] Treatment decisions (i.e. to treat them surgically or to follow them medically) are often challenging in patients with less severe forms[1,2,8,9] who are often asymptomatic and who might be diagnosed incidentally.

According to our data, the overall survival of patients with SS is high, and the majority of our patients are asymptomatic at the late clinical examination. Notably, the success of surgery was related to the age of patients. Patients requiring surgical treatment under 1 year of age are usually very ill, and have a relatively high-operative mortality and complication rate, whereas older patients have a better outcome both immediately and in the long term. Surgically treated patients had a significant higher proportion of simple CHD compared with CMP (mainly ASD); this could be an explanation why there was a higher left-to-right shunt and the reason why these patients were diagnosed and operated earlier. We found that surgical treatment is beneficial in reducing symptoms and it reduces the risk of developing late symptoms. The therapeutic occlusion of any significant anomalous SAS to the right lung[30] significantly improved the clinical status of patients with congestive heart failure, thus postponing the need for surgical treatment.

Pulmonary hypertension and the presence of associated CHDs, in particular complex CHDs, were negative prognostic factors in the survival of patients, irrespective if patients were treated surgically or followed in their natural history. Pulmonary hypertension was found in more than one-third of our patients, and it was mostly seen in patients with associated CHDs, showing a correlation among these variables. Nonetheless, even patients with isolated SS may present with pulmonary hypertension.

Even considering the good results of surgery, we found that SS corrective surgery is not complication-free, and almost 25% of our STPs had scimitar vein-related morbidities (i.e. stenosis/occlusion of the scimitar drainage), which in most cases (more frequently in neonates/infants than in older patients) required additional surgical or haemodynamic interventions. Given the not negligible associated early and late morbidities in STPs, we suggest that surgical redirection of the anomalous pulmonary venous drainage in patients with isolated SS should be considered only when the scimitar drainage causes considerable pulmonary overload (Qp:Qs > 1.5:1) (*Figure 5*). We believe that in selected patients, the correction of associated CHDs together with the therapeutic occlusion of SAS to the lung may be beneficial, and so avoid or postpone the need for surgical correction of SS to an older age (especially in asymptomatic patients), and so decrease the risk of late morbidities.

Based on this study, we suggest that patients with SS undergo continuous clinical and non-invasive monitoring (with MRI) to identify clinical or physiological variations in order to administer timely appropriate treatment and to check postoperative outcomes. Cardiac catheterization can be avoided in patients without intra- or extracardiac shunts; however, it is necessary when pulmonary hypertension is suspected.

Limitations

This is a retrospective multi-centre data collection study, and inter-institutional and intra-institutional variability of treatment strategies cannot be excluded. In addition, the presence and degree of right lung hypoplasia and right ventricular dilation were both qualitative evaluations being based on the physician's experience, and may vary between centres. Moreover, the median age at last follow-up control

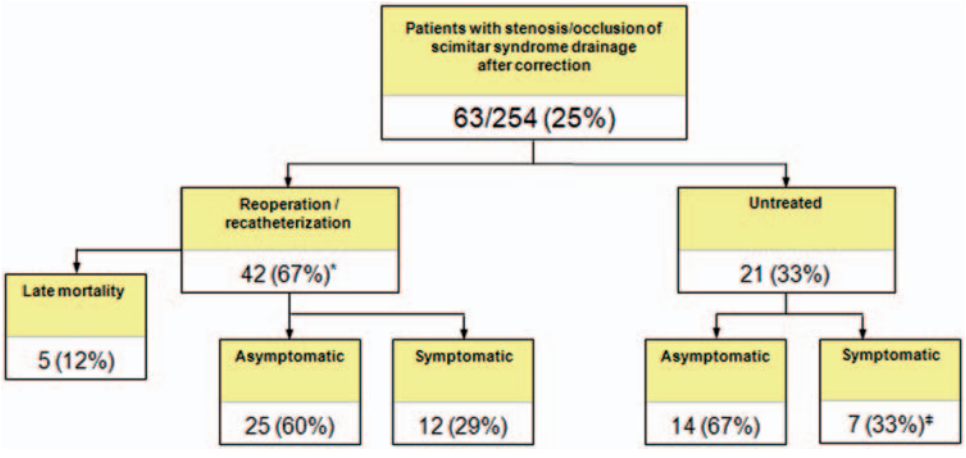

Figure 4 Flowchart showing the outcome of patients with postoperative scimitar vein stenosis/occlusion. *Two patients required a right lung lobectomy. ‡Four patients refused any additional treatment, and three patients are currently clinically monitored.

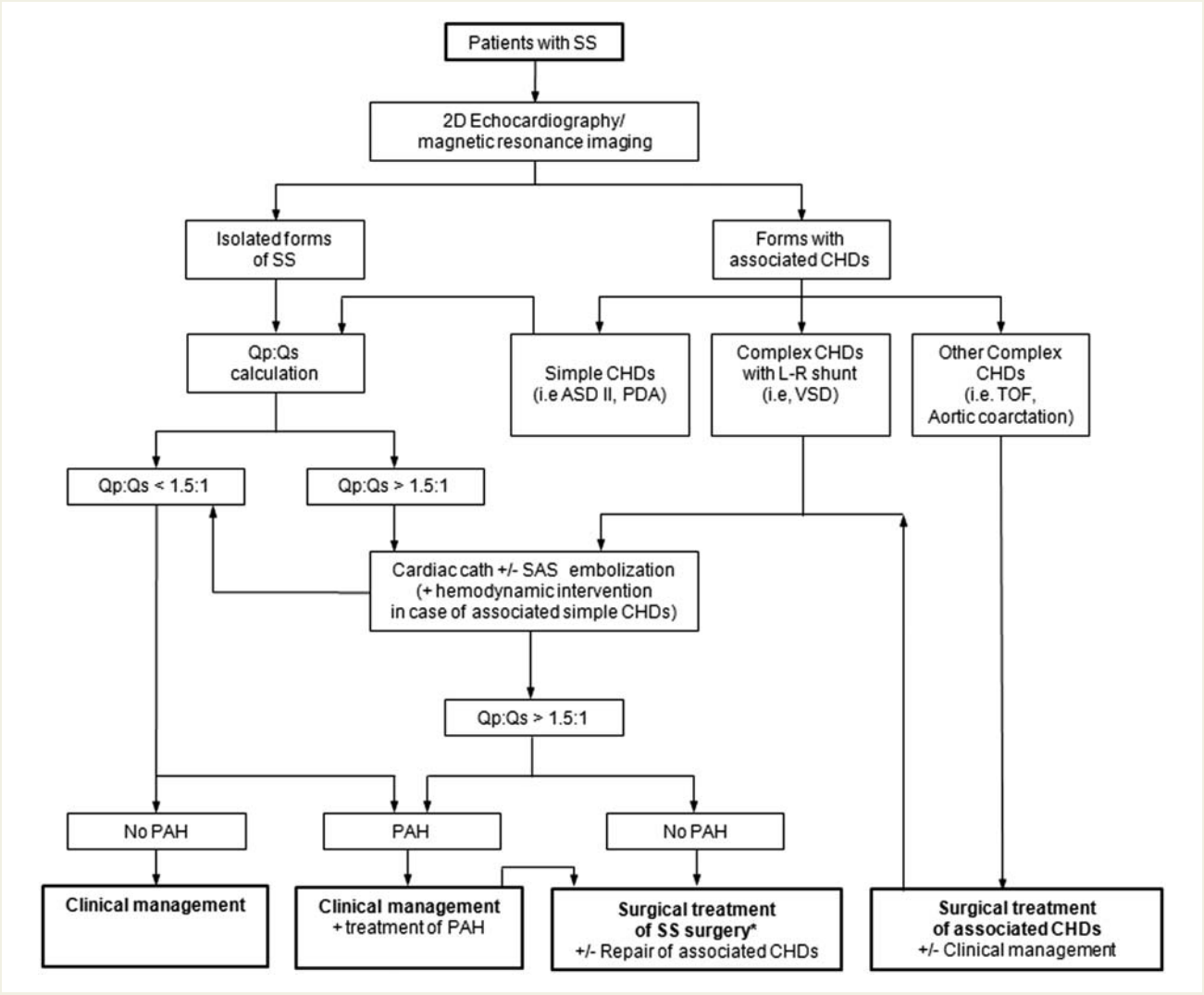

Figure 5 Flowchart showing our therapeutic management plan for patients with scimitar syndrome (SS). ASD II, atrial septal defect ostium secundum type; CMTs, clinically monitored patients; PAH, pulmonary arterial hypertension; Qp:Qs, pulmonary-systemic blood flow ratio; PDA, patent ductus arteriosus; SAS, systemic arterial supply; STPs, surgically treated patients; TOF, tetralogy of Fallot; VSD, ventricular septal defect. *High risk for late stenosis/occlusion of the scimitar drainage in neonates/infants.

was higher in STPs than in CMPs, although we adjusted for age using the propensity score model. Lastly we have no or limited information on functional class, imaging parameters on right ventricular dilatation and function, and arrhythmias.

Conclusions

We report the outcome of the largest series of SS patients hitherto evaluated. We conclude that the overall survival of patients with SS is high, and survival probability is lower in patients with associated CHDs and in patients with pulmonary hypertension. Surgical treatment of SS is beneficial in reducing symptoms. Surgical repair is indicated in symptomatic patients and in patients with significantly increased pulmonary blood flow. In asymptomatic patients, it must be tailored to a comprehensive haemodynamic evaluation (i.e. proved considerable pulmonary overload of the scimitar vein drainage) and to the patient's age because there is a high risk of developing postoperative scimitar drainage stenosis/occlusion.

We believe that in selected patients, correction of associated CHDs together with the therapeutic occlusion of SAS to the lung may be beneficial, and so avoid or postpone the need for surgical correction of SS to an older age, and so decrease the risk of late morbidities. A continuous follow-up is indicated.

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Supplementary material

Supplementary material is available at *European Heart Journal* online.

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