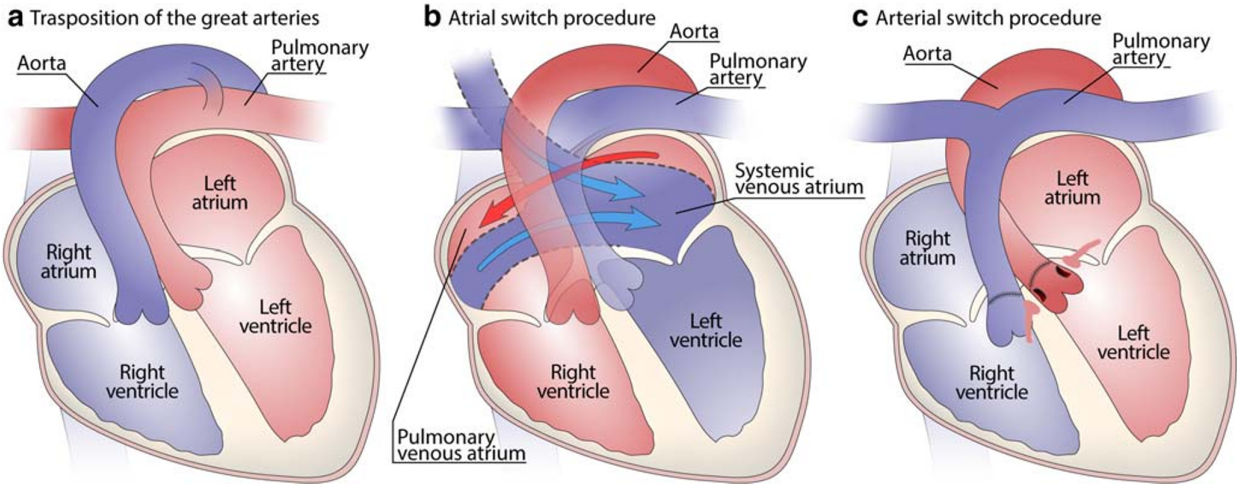

Fig. 7 Transposition of the great arteries **(a–c)**: Drawing of the native defect, with the aorta originating from the RV and the pulmonary artery from the left ventricle **(a)**. Drawing of the atrial switch (Mustard or Senning procedure), redirecting the systemic venous blood flow into the left ventricle and the pulmonary trunk, and the oxygenated blood from the lungs into the right ventricle and the aorta **(b)**. Drawing of the arterial switch procedure with repositioning the great vessels above the appropriate ventricles and re-implantation of the coronary arteries **(c)**

Autopsy recommendations

Evaluate the size of the aortic arch and isthmus, the thickness of the aortic wall at the site of narrowing. Look for signs of hypertension in the upper part of the body (atherosclerosis of the large- and medium-size arteries), LV hypertrophy, congestive heart failure, coronary artery disease, stroke, endarteritis, cerebral berry aneurysms, and aortic dissection. Histopathological features observed in the unoperated CoA include disorganized or fragmented elastic fibers, extracellular mucoid medial accumulation (MEMA) [45], and in adults myofibroblastic proliferation and atherosclerosis.

In case of death early after repair, lacerations of the aortic wall, adventitial hematomas, and thrombosis/thromboembolism should be sought for. Late after repair, false aneurysm and infectious endarteritis (with associated embolic risk), at the site of repair may be encountered (Table 1, Tables S2 and S3 supplement).

Complete transposition of the great arteries (D-TGA)

Description: Anatomically, the combination of concordant AV connections (the atria are connected to the correct/respective ventricles) and discordant VA connections (the ventricles are connected to the incorrect great arteries) results in systemic venous return being sent to the systemic circulation and pulmonary venous return sent back to the lungs (Fig. 7A).

For survival, a large ventricular or atrial communication is, thus, necessary to allow mixing of blood [46]. Over 60% of cases occur in isolation and require early atrial septostomy; the remaining are associated with other congenital defects, mainly VSD or obstruction of the (subpulmonic) left ventricular outflow tract (LVOT) or both (30%). Most commonly, the aorta is located in right anterior position relative to the pulmonary trunk.

In the absence of a large interatrial (ASD) or interventricular communication (VSD), the newborn with complete transposition usually succumbs rapidly upon closure of the oval fossa and the arterial duct due to severe desaturation of the arterial blood. This requires immediate surgical palliation by means of balloon atrial septostomy (Rashkind procedure [47, 48]) to improve hypoxemia. Permanent surgical correction can be achieved at a second stage by means of either *atrial switch procedure* (so-called physiological correction, Mustard [49] or Senning procedure [50], currently abandoned) (Fig. 7B) or, nowadays, *arterial switch procedure* (anatomical correction, Jatene procedure, (Fig. 7C) with excellent early and late-term survival and outcomes) [51] (Fig. 8) (Tables 1 and 2).

Autopsy recommendations

At autopsy, adult patients are nearly always repaired, and pathology relates to the type of surgical procedure undertaken. *Arterial switch procedure* is presently the preferred choice and performed ideally within 2 weeks from birth. Aorta and pulmonary trunk are transected close to their valves for re-implantation; hence, the pulmonary valve becomes the "neo-aortic" valve, and the aortic valve becomes the neo-pulmonary valve. This procedure also requires (microsurgical) retrieval of the proximal coronary arteries, with re-implantation of their ostia over the neo-aortic valve. In addition, the procedure includes the reconstruction of the pulmonary trunk with pericardial patch (Table 2). Long-term complications include aortic

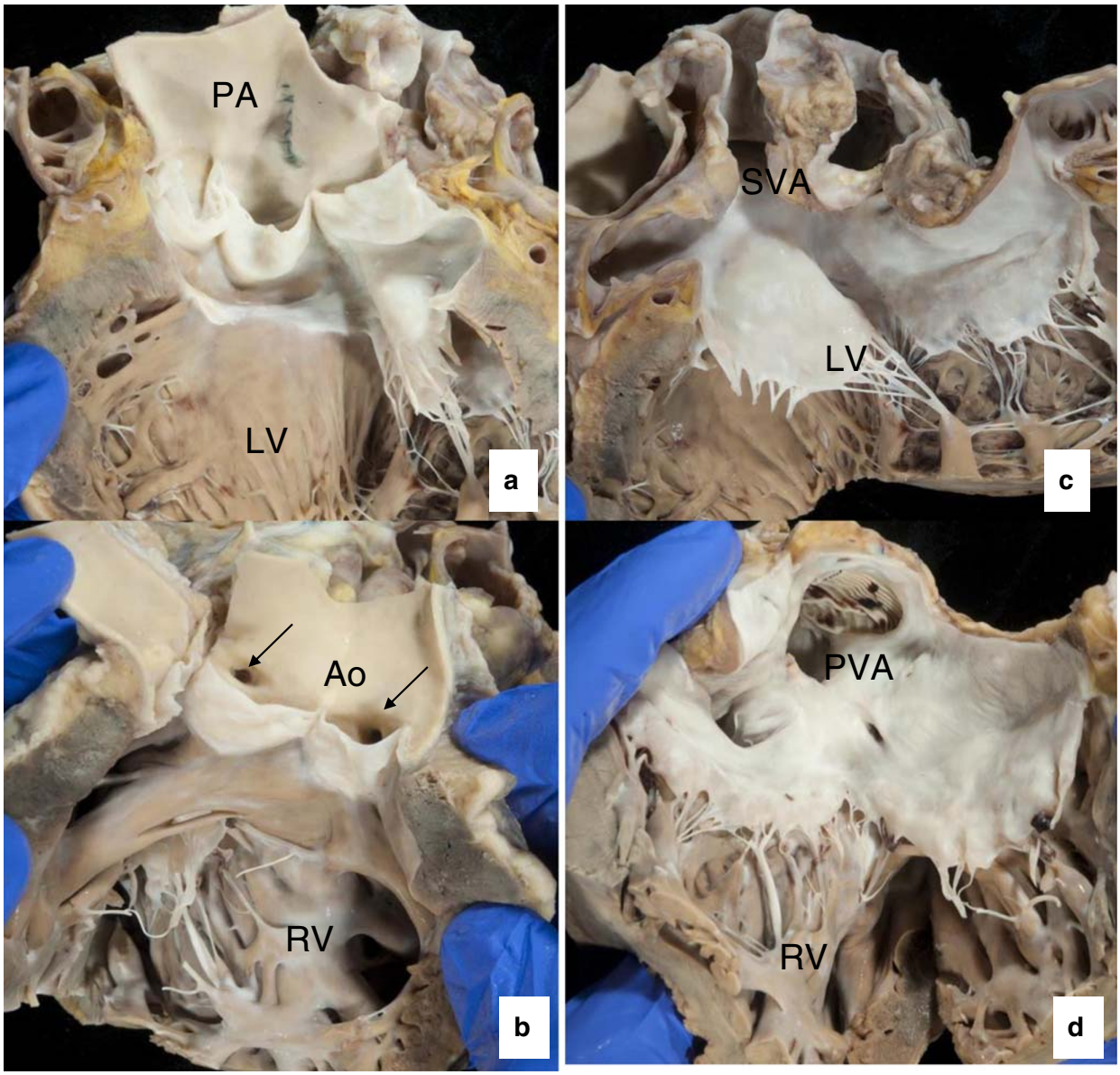

Fig. 8 Transposition of the great arteries after Mustard correction at adult age **(a–d)**. Outflow tract of left ventricle is connected to the pulmonary artery **(a)**. Outflow of the right ventricle is connected to the aorta, with "anomalous" origin of the coronary arteries **(b)**. Anterior (atrial) baffle directing the caval blood toward left ventricle **(c)**. Pulmonary venous baffle (with prosthetic material visible) directing blood toward the tricuspid valve and right ventricle **(d)**

root dilatation with possible aortic valvar insufficiency, left ventricular failure, and myocardial ischemia. RVOT obstruction, and stenosis of branching pulmonary arteries, can occur when the pulmonary trunk had to be repositioned anterior to the aorta (LeCompte procedure). Inspection of coronary ostia and proximal course of the coronary arteries (scarring) is important to rule out kinking and/or acquired atresia.

The atrial switch procedure (Mustard or Senning) (Fig. 7B, Table 2) is now largely abandoned in favor of arterial switch (Fig. 7C) and is commonly encountered in older adults with D-TGA. This procedure includes resection of the atrial septum, which is replaced by a "baffle" that channels the superior and inferior caval blood to the pulmonary circulation via the subpulmonary left ventricle, whereas the pulmonary venous blood is channeled from behind the baffle toward the tricuspid valve and systemic RV and tricuspid valve.

On autopsy, severe hypertrophy and dilatation of the RV are observed, with tricuspid insufficiency and deviation of the septum toward the LV unless LVOT obstruction is present. Surgical

Table 2 Most important types of systemic to pulmonary artery shunts and definitive repairs

Blalock-Taussig shunt	Subclavian artery directly anastomosed to pulmonary artery (right or left)
Modified Blalock-Taussig shunt	Conduit of synthetic material between subclavian artery and pulmonary artery
Mee procedure	Ascending aorta to main pulmonary artery
Waterston shunt	Ascending aorta to right pulmonary artery
Potts shunt	Descending aorta to left pulmonary artery
Standard ToF repair	Closure of the VSD and relief of the pulmonary/RVOT stenosis
Variants of ToF repair	Right atrial approach versus right ventriculotomy preserving PV versus transannular patch
Rastelli procedure	A Gore-Tex patch tunneling the lef ventricle to the aorta, closing the VSD. The pulmonary valve is surgically closed and an artificial conduit and valve from the right ventricle to the pulmonary bifurcation
Atrial switch procedures (Mustard or Senning)	A two-way baffle in the atria connects the SVC and IVC to the left ventricle and the PV to the right ventricle. In a Senning procedure, the baffle is made with pericardium of the pt.; in the Mustard procedure, a synthetic material is used
Arterial switch (Jatene operation)	The left and right coronary arteries are removed from the Ao and re-anastomosed to the adjacent pulmonary artery, which was to become the neo-aorta, and by transecting and transposing the aorta and main pulmonary artery
Da Silva	Extensive leaflet mobilization, longitudinal plication of the atrialized ventricle, and cone-shaped reconstruction of the tricuspid valve, allowing for leaflet-to-leaflet co-aptation.
Glenn	The SVC is connected to the right pulmonary artery
Fontan	Direct atriopulmonary connection (right atrial appendage to pulmonary trunk which has been detached from the pulmonary valve)
Fontan modified	The IVC is disconnected from the heart and inserted into the pulmonary artery. A conduit can be interposed between the IVC and the PA and can be fenestered. The right ventricle become the systemic ventricle connected the Ao. The SVC is connected to the PA

damage to conduction system, extensive fibrosis due to ventricular remodeling of the RV, and atrial scarring due to surgery are substrates for the frequently occurring atrial and ventricular arrhythmias and instances of sudden death. In addition, the presence of baffle stenosis or leaks must be evaluated, occurring in a quarter of patients. Finally, the presence of endocarditis should be assessed.

Cases of unrepaired TGA, typically with a large VSD, are rare in adult life and are typically associated with Eisenmenger syndrome, in the absence of pulmonary stenosis, i.e., severe pulmonary vascular disease (Tables 1 and 2, Tables S1, S2 and S3 supplement).

Congenitally corrected transposition of great arteries (CCTGA)

Description: Discordant atrioventricular and ventriculo-arterial connections (double discordance) result in a "physiologically correct" circulation through the heart in the absence of associated defects.

However, long-term outcome depends on adaptation of the RV and tricuspid valve to support the systemic circulation, similar to what was described for TGA patients after atrial switch repair [52]. Commonly associated defects include a VSD, pulmonary stenosis, and "Ebstein-like" malformation or other tricuspid valve pathology (15–80%) causing regurgitation [53]. In the absence of associated defects and a well-adapted systemic RV, ccTGA can remain asymptomatic for decades and may be diagnosed very late in life or at autopsy. However, the intrinsic abnormality of the AV conduction system, with the AV node aberrantly located anteriorly and the His bundle on the pulmonary outflow, puts ccTGA patients at risk of wear and tear injury, which explains onset of AV block and cardiac arrest. Reportedly, one half of this patient population requires a pacemaker [54] (Table 1).

Autopsy recommendations

Autopsy should start with establishing the viscero-atrial situs, atrioventricular and ventriculo-arterial connections. The position of the aorta in relation to the pulmonary trunk should be recorded, as well as eventual associated lesions. The wall of the morphologic (subpulmonary) LV is typically thin, while the morphologic (systemic) RV is dilated and severely hypertrophied. Tricuspid regurgitation with either abnormal valve leaflets (Ebstein-like) or due to annular dilatation is a frequent complication in the adult, with right ventricular (systemic) failure occurring in patients > 50 years or earlier and an increased risk of endocarditis.

When examination of AV conduction system is required, it should be noted that, in hearts with situs solitus, the coronary sinus and triangle of Koch are not a point of reference for sampling tissue blocks (Table 1).

Ebstein anomaly of the tricuspid valve

Ebstein anomaly (EA) is rare (< 1% of all CHD cases). It usually occurs sporadically, but familial cases have been reported.

Description: The anatomical hallmark is displacement of the tricuspid hinge line (annulus) toward the RV apex affecting the septal and posterior leaflets.

This apical displacement of the valve results in the pretricuspid part of the RV becoming "atrialized" and thin-walled [55]. Ebstein anomaly is often associated with an atrial septal defect or patent foramen ovale, which may allow left to right shunting and cause systemic desaturation. Wolff-Parkinson-White syndrome (WPW) is present in up to 30% of patients. RV outflow tract obstruction is more often observed in young patients.

Symptoms depend on the severity of tricuspid regurgitation and size of the "functional" RV. This size is variable but can be limited to the outflow tract only, which then becomes dilated and hyperdynamic. Accordingly, the clinical presentation may vary from asymptomatic in very mild cases to deep cyanosis and heart failure (mostly in neonatal cases). Arrhythmias are common in adult life, and there is an increased risk of sudden death [56]. Wolff-Parkinson-White syndrome (WPW) is associated in up to 30% of patients.

Surgical repair with implication of the atrialized portion of the RV and closure of associated septal defects is the preferred option. Currently, the most commonly used technique is the "cone" reconstruction technique described by Da Silva, [57] (Table 2), which creates a cone-looking tricuspid valve from the available leaflet materials [58]. Rarely, when reconstruction is impossible, the valve is replaced with a bioprosthetic valve. Some patients may also undergo bidirectional Glenn anastomosis (anastomosis of the superior vena cava to the right pulmonary artery) to reduce RV preload and the risk of heart failure (Table 1).

Autopsy recommendations

Patients presented at autopsy can be either operated at young age (infants, severe disease), operated at older age, or not operated at all. Typically, dilatation of the RV, tricuspid valve annulus, and functional RV is observed. The valve annular dilatation can reach 20 cm and is best visualized via an atrial view, followed by opening of the RV outflow, from the apex to the pulmonary valve. From this incision, the cone reconstruction can be visualized optimally. The displaced leaflets, which have dysplastic appearance, are usually attached to the ventricular wall; the annular attachment of the anterior leaflet is normally located, but the leaflet is often dysplastic and abundant (sail like). Complications include infective endocarditis

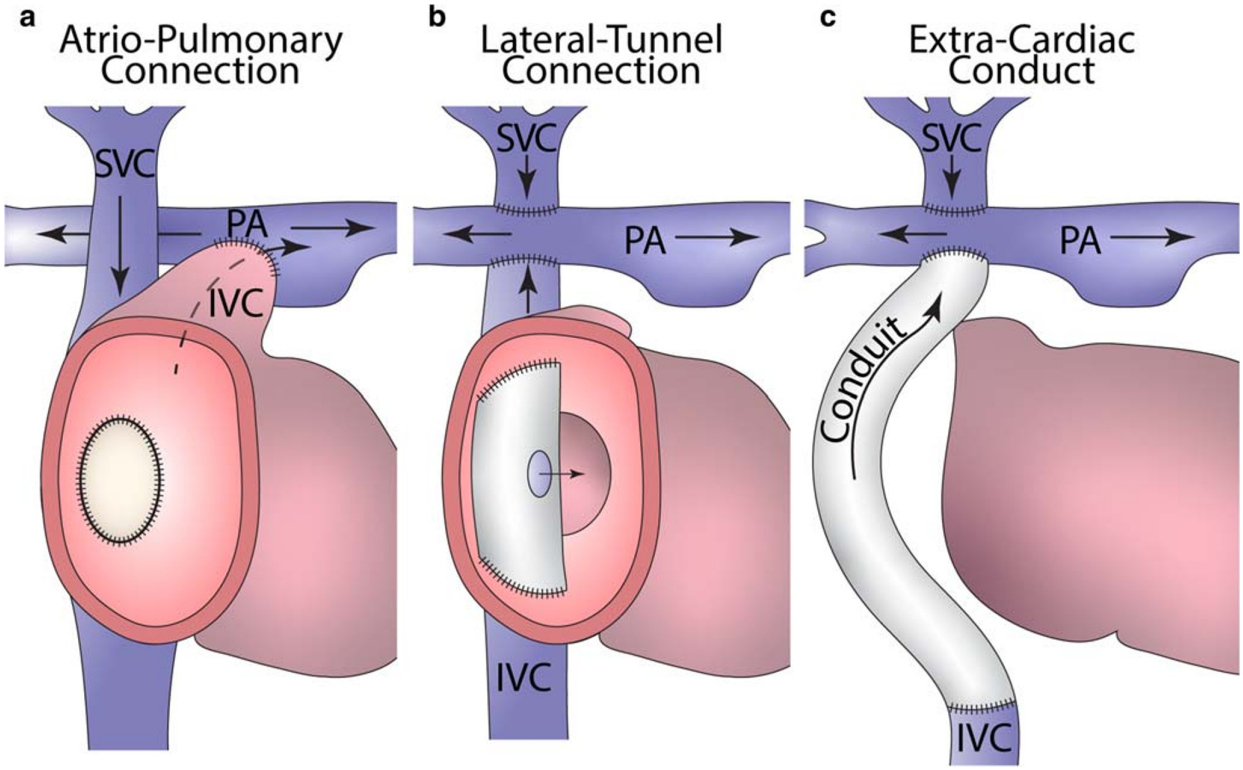

Fig. 9 The different types of Fontan-type procedures, grouped in main patterns **(a–c)**. Direct atriopulmonary connection without interposition of conduits **(a)**. Intracardiac lateral tunnel draining the IVC into the pulmonary circulation bypassing the right ventricle **(b)**. Extracardiac conduit draining the IVC blood into the pulmonary arteries **(c)**. In **(b)** and **(c)**, a bidirectional Glenn anastomosis drains SVC blood to the right pulmonary artery

(operated and non-operated cases), systemic emboli, and pathology related to ablation of arrhythmias (WPW syndrome) or degeneration of a prosthetic valve. Not infrequently, left-sided heart pathology can also be present: ventricular dilatation, fibro elastosis, and left ventricular fibrofatty substitution. Other valvar abnormalities, such as mitral valve prolapse and a bicuspid aortic valve, have been reported (Table 1).

Anomalous pulmonary venous connections (return)

Description: One or more pulmonary veins connect to a site other than the morphologically left atrium.

It can be *total* (diagnosed and repaired early in life) or *partial*, when a solitary vein or all the venous connections from one lung drain into the right-sided atrium or the superior vena cava. Most frequently in adults, the right pulmonary veins drain into the superior vena cava, often associated with the sinus venosus ASD, or the right pulmonary veins drain into the right-sided atrium. In the "scimitar syndrome," one or two right-sided pulmonary veins "pierce" the diaphragm and drain into the inferior vena cava, and there is dextroposition of the heart because of hypoplasia of the right lung; part of the lung can be sequestrated in terms of its bronchial supply; anomalous pulmonary arterial supply through systemic collateral arteries derived from the descending aorta. In other cases of partial anomalous pulmonary venous connection, the left pulmonary veins drain into the common venous truncus so that the blood enters the right atrium. The presence of an ASD allows the survival of patients with total anomalous pulmonary venous connection, with blood shunting the systemic circulation.

The timing of surgery depends on the severity of obstruction to venous return and oxygen saturations. Partial anomalous connections of the pulmonary veins may be of little functional significance and can be an incidental finding or can become symptomatic later in adulthood. Surgical repair "reroutes" pulmonary venous return to the left atrium using an autologous pericardial patch to create a tunnel in the right atrium through the ASD (Table 1).

Autopsy recommendations

In surgically treated adult patients, the pathologist should exclude pulmonary venous obstruction and residual lesions. In cases of scimitar syndrome, the inferior vena cava should be examined, as well as bronchial and pulmonary arterial supply to the right lung. In unrepaired cases, left to right shunting typically results in right heart dilatation. Histology of the lung vasculature is required to exclude pulmonary vascular disease (Table 1).

Univentricular hearts after a Fontan-type procedure

Named after Francis Fontan, a brilliant French surgeon who invented the procedure in 1968, the Fontan procedure and the many modifications over the years are palliative surgical

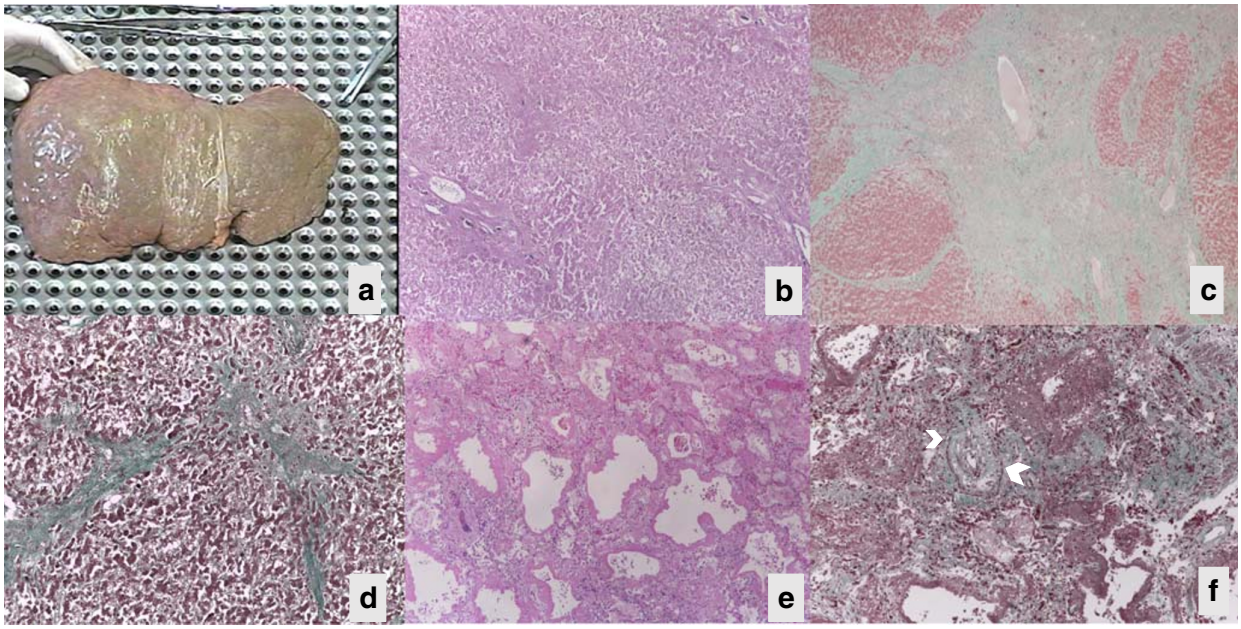

Fig. 10 Failing Fontan circulation with hepatic cirrhosis and pulmonary hemorrhage **(a–f)**: macroscopic view of the liver at autopsy, with evidence of cirrhosis **(a)**; histology showing fibrosis with disorganization of the structure, dilatation of the veins, and regenerative nodules using hematoxylin-eosin staining **(b)**; Masson trichrome staining highlighting the fibrosis in green **(c)**; high-power view of c **(d)**; lung hemorrhage, hematoxylin and eosin staining **(e)**; lung thrombosis (white arrows), Masson trichrome staining **(f)**