Unifocalization cannot rely exclusively on native pulmonary arteries

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Unifocalisation Cannot Rely Exclusively on Native Pulmonary Arteries: the Importance of Recruitment of Major Aortopulmonary Collaterals in 249 cases.

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Key Question: How does the nature of the pulmonary vasculature impact on technique and survival in pulmonary atresia/VSD/MAPCAs?

Key Findings: Unifocalisation can be achieved in 90% of cases but the need to leave VSD open is associated with poorer late survival

Take-Home Message: Combination of Rehabilitation and Recruitment Strategy achieves high unifocalisation rates

Abstract:

Objectives: To define the early and late outcomes of unifocalisation based on a classification of the native pulmonary artery(nPA) system and Major Aortopulmonary Collateral Arteries(MAPCAs) with a policy of combined recruitment and rehabilitation. To analyse the role of unifocalisation leaving the VSD open with a limiting right ventricle-pulmonary artery conduit in borderline cases.

Methods: Analysis of 271 consecutive patients assessed for unifocalisation at a single institution between 1988-2016. Patients classified according to the pulmonary blood supply: Group A, unifocalisation based on nPA only; Group B, based on nPA and MAPCAs; Group C, MAPCAs only(absent nPAs).

Results: Unifocalisation was achieved in 249(91.9%) cases with an early mortality of 2.8%. Group A included 72(28.9%) patients, Group B 119(47.8%) patients and Group C 58(23.3%) patients with no difference in early survival between groups. Survival at 5, 10 and 15 years was 90.0%(85.9 to 94.3), 87.2%(83.5 to 91.2) and 82.3%(75.2 to 89.9). Late survival in Groups A and B was similar but 10 and 15 year survival in Group C was decreased at 79.2%(68.2 to 92.1) and 74.3%(61.1 to 90.4) (p=0.02). A mean of 1.9(±0.6) MAPCAs were recruited per patient (range 0-6).

The VSD was left open with a limiting RV-PA conduit in 97(39.0%) cases, but subsequently closed in 48, giving, a total of 200(80.3%) achieving VSD closure(full repair). Delaying VSD closure was not associated with increased risk for early or late survival.

A central shunt to rehabilitate the nPAs was used in 56(22.5%) cases. This was associated with a reduction in the number of MAPCAs recruited, but still required a mean of 1.8(±0.5) MAPCAs recruited per patient to achieve unifocalisation.

In multivariate risk analysis, those suitable for single stage full repair had the best long term outcomes. Group C anatomy was associated with poor late survival compared to Groups A and B (hazard ratio2.7).

Conclusion: Survival is maximized by a combined approach of rehabilitation and recruitment. MAPCAs should always be recruited if they supply areas with absent nPA supply. A strategy of leaving the VSD open with a limiting RV-PA conduit is a safe and effective way of managing borderline cases.

Introduction

Pulmonary atresia with ventricular septal defect(VSD) and major aortopulmonary collateral arteries(MAPCAs) is a complex and rare (10 of 100,000 livebirths[1]) condition, characterized by a heterogeneity of pulmonary blood flow derived from multiple sources that vary in number, size, distribution and origin, as well a variable relationship between the MACPAs themselves and the native pulmonary artery(nPA) system[2-4]. This great variability means that a single strategy or technique will not suit all patients, but the importance of '*unifocalisation*' of all pulmonary blood flow to a central source has become widely accepted as the primary goal.

Surgical strategies are evolving that have dramatically improved the prognosis– but there remains controversy regarding the ideal approach to achieve the best long-term outcomes.

This study addressed three key areas of this controversy: (a) having achieved unifocalisation, when should the VSD be left open or closed, (b) the relative contribution of MAPCAs versus native PAs in achieving unifocalisation, (c) the role of rehabilitating native PAs prior to unifocalisation. There also continue to be differing opinions over specifics of surgical technique such as sternotomy alone verses sternotomy and thoracotomy [5,6]. One philosophy of management is to rely predominantly on native PAs alone but the majority of reports (including our own) favour recruitment of MAPCAs wherever possible, in tandem with the native vessels [7]. Key to this strategy is the recognition of the concept of 'dual supply' where the same region of pulmonary vascular bed is supplied by both the nPA system and by MAPCAs.

Materials and Methods

Data on all patients with pulmonary atresia, VSD and MAPCAs who underwent surgical intervention at Birmingham Children's Hospital, United Kingdom, between January 1988 and December 2016, were reviewed. Angiograms and operative details were available for all patients and hospital records for all interventions and follow-up. Patients referred from overseas (12%) were followed up locally, with current status obtained for 98% of cases. The study was registered with our institutional Research & Development office; in accordance with the UK NHS National Research Ethics Service guidance, neither individual informed consent nor formal Research Ethics Committee review was required, because the study was undertaken using information previously collected in the course of routine care.

Patients with other intra-cardiac pathologies accompanied by MAPCAs were excluded from the study. A total of 271 patients were included, of which 53(19.6%) patients had been referred to us after initial palliation in a different centre.

Assessment: All patients underwent extensive angiography including pulmonary vein wedge injections followed by CT angiography or MRI to define the three-dimensional anatomy and the relationship to the airways and oesophagus (Our institutional preference is for CT angio but MRI can be used especially if functional information on the heart is required). A roadmap of the pulmonary vasculature was created, establishing the origin, size and distribution of each MAPCA as well as the presence, size and extent of any native PAs. It was particularly important to identify areas of the lung with dual supply.

The primary aim was to achieve unifocalisation of all accessible pulmonary vessels at a single stage. Native PAs were used wherever possible but all MAPCAs supplying one or more segments of the lung were recruited as part of the surgical strategy, unless there was clear evidence of dual supply (in which case they were ligated). The lung fields were divided into their 20 broncho-pulmonary segments and operative strategy was to close the VSD if 15 or more lung segments could be recruited. This involved careful assessment of all AP and lateral injections of each MAPCA to create as accurate an estimate as possible. If <15 could be recruited then the VSD was left open - placing a limiting RV-PA conduit to prevent overcirculation. If vessels were found to be of poorer quality than expected at time of surgery, or if MAPCAs could not be accessed, then the strategy reverted to leaving the VSD open. We prefer this to leaving a fenestrated VSD, which can be difficult to judge if the pulmonary vascular resistance changes over the early post-operative period.

The unifocalisation strategy was categorized into 3 groups defined as follows::
Group A – unifocalisation based on native PAs only,
Group B – unifocalisation with a combination of native PAs and MAPCAs
Group C – unifocalisation with MAPCAs only i.e. absent native PAs.

Patients presenting with confluent but small/diminutive central PAs and MAPCAs that were inadequate to achieve the target of 15/20 perfused segments underwent creation of an AP window to drive antegrade flow into these vessels (sometimes referred to as the 'Melbourne Shunt' as described by Watterson et al [8]). These patients subsequently fell into groups A and B, and the use of this central shunt/AP window was factored into the analysis. Wherever possible, these central shunts were performed without bypass, but if the aorta did not tolerate the necessary partial clamping and distortion, then bypass was used to provide stability.

Surgical approach: The technical aspects of our approach to unifocalisation have been described previously and can be summarized as follows (figs 1 and2)[9-11]: The preferred approach was midline sternotomy alone. However, initial thoracotomy was used when access to MAPCAs from the midline was likely to be difficult or if MAPCA anastomosis(es) could be better performed via thoracotomy.

At sternotomy, all vessels were mobilised and controlled, often working through the posterior pericardium between the aorta and SVC to develop vessels lying under the carina and along the underside of the main bronchi. Cardiopulmonary bypass was established and the origins of all MAPCAs ligated. Vessels were controlled distally with Yasargil® clips, divided at their origins and laid open along their length to reach maximum calibre. Native PAs were laid open out onto their branches to create a 'platform' of native tissue onto which the individual MAPCAs were attached. If no native PAs were present then larger MAPCAs were brought together across the midline to create this platform. The reconstructed platform of focalized vessels was then patched over with a large piece of pulmonary homograft(with separate patches into individual vessels if necessary). In Group A the feeding MAPCA vessels were ligated and the repair was based on the native PAs, which were laid open from hilum-to-hilum, and out into their branches if necessary before being reconstructed as above.

A defect was then cut into the homograft patch to receive the RV-PA conduit. Conduits used were either aortic homografts or Hancock® valved tube grafts. If there was inadequate tissue across the midline, ipsilateral vessels were focalized at each hilum and then patched together with pulmonary homograft; a Goretex® tube graft was then used to connect these two sets of vessels together and the RV-PA conduit connected to this tube as a T-graft.

If the VSD was to be left open, then limiting conduits were selected at a diameter to be the predicted half-size +2mm based on the patients' body surface area. If necessary these could be externally clipped with ligaclips to limit the intraluminal diameter to the desired point. Dacron valved conduits were used as these could be sure to maintain their dimensions under high pressure. Our techniques share common features of repairs reported by other centres[5,12].

Statistical methods:

Data are presented as counts and percentages or for continuous values as median and interquartile range (Q1-Q3). Demographic characteristics were compared using the Kruskall–Wallis test or the Chi-Square test.
Short-term mortality is calculated based on status at 30-days post repair. Estimates of survival were made using the Kaplan–Meier method, using mortality as the event. Survival between groups was compared using the log-rank test. A Cox PH model was created to look at risk factors for mortality. The age at repair over time is presented as a Locally Estimated Scatterplot Smoother (LOESS) plot.
Statistical analyses were performed with R version 3.5.1 (R Core Team, 2018).

Results

A total of 271 consecutive patients were included in the study. Unifocalisation was achieved in 249(91.9%) of cases(table 1). The remaining 22(8.1%) cases either had such poor vasculature that they were not suitable for unifocalisation(18, 6.6%) or are currently awaiting planned unifocalisation(4, 1.5%). These patients have been palliated with shunts and/or stents to individual vessels.

Group A – unifocalisation was based on native PAs only(72, 28.9%),
Group B – unifocalisation based on a combination of native PAs and MAPCAs(119, 47.8%)
Group C – unifocalisation using MAPCAs only(58, 23.3%).

A total of 789 MAPCAs were defined in the group of 249 cases, in which a mean of 1.9(±0.6) MAPCAs were recruited per patient (ranging from 0 to 6). A total of 268 MAPCAs were ligated at the time of surgery due to there being dual supply. The numbers of MAPCAs recruited and ligated are summarised in table 2. When comparing Groups B and C, significantly more MAPCAs were recruited per patient in Group C(p=0.01), but the ratio of recruited:ligated MAPCAs was similar in both groups (p=0.57).

The median age of patients at time of unifocalisation in the entire study was 23 months. There was no statistical difference in mean age across the three groups, although those in Group C were the youngest, at a median of 18 months. The median age at unifocalisation

has reduced over the period of the study, having been 44.3 months in the initial quartile and 18.0 months in the last quartile(table 1). A LOESS line plot depicting the distribution of ages of the entire series is provided in the supplementary data(Supplementary Fig.1).

In terms of the surgical approach used, 91(36.5%) patients were unifocalised utilising median sternotomy alone and 158(64% patients) using combined thoracotomy and median sternotomy. There was no difference in survival at 5, 10 or 15 years between these two groups(p=0.58).

Early (30 day and in-hospital) mortality was 2.8%(7 patients) with no early deaths in the last 12 years of the study. Survival of the entire group is shown in figure 3a with 5, 10 and 15 year survival of 90.0%(85.9 to 94.3), 87.2%(83.5 to 91.2) and 82.3%(75.2 to 89.9). There was no difference in early survival between the three groups(table 1, p=0.10). Kaplan-Meier survival curves for the three groups of patients in shown in figure 3b. Survival of Groups A and B were very similar and the combined A and B patients had a 10 and 15 year survival of 89.6% (84.1 to 95.6) and 84.7% (76.6 to 93.7). However, late survival of Group C patients(absent native PAs) was significantly worse than Groups A and B combined, with 10 and 15 year survival of 79.2%(68.2 to 92.1) and 74.3%(61.1 to 90.4) (p=0.02).

Central ('Melbourne') shunt: By definition, these patients were all in Groups A and B. A total of 56(22.5%) patients underwent a central shunt, with 45(80.4%) in Group B and 11(19.6%) in Group A. Figure 4 shows the outcomes of unifocalisation in patients who required initial central (Melbourne) shunt verses those undergoing single stage repair with no difference in early or late survival between the groups(p=0.62). Within Group B, the mean number of recruited MAPCAs was 1.8(±0.5) in the Melbourne-shunt patients compared to 2.5(±0.7) who had single stage unifocalisation. The ratio of recruited: ligated MAPCAs was 2.05 in the Melbourne-shunt group compared to 2.75 in the single-stage group(p=0.05).

Status of the VSD: open or closed: The VSD was closed at the primary procedure in 152(61.0%) cases. The corollary of this is that the VSD was left open with a limiting conduit in 97 (39.0%) patients, in whom, the VSD was subsequently closed at a second procedure ('delayed VSD closure') in 48 of the 97(49.5%). Overall, a total of 200(80.3%) cases achieved VSD closure (full repair) during the period of this study.
In the analysis of the remaining 51 patients, complete repair is predicted in a further 8 cases. This leaves 43(17.3% of the total cohort) cases where the vasculature is felt to never be suitable for VSD closure and this is likely to be their final status.

There was no difference in early mortality between the group in whom full repair was achieved and those in whom the VSD was left open. The VSD was left open initially in 29% of Group A patients compared to 43% in Group B and 38% in Group C (p=0.13). There was also no difference in the frequency of VSD closure between Groups A, B or C (table 1). There were two patients in whom the VSD was initially closed, but had to be fenestrated within the first 24 hours due to high RV pressures. One of these patients was an early death with progressive heart failure and the second was able to have the VSD fully closed at a subsequent procedure.

Survival curves according to VSD status are shown in figure 5(a and b). Patients in whom the VSD has never been closed had a significantly worse survival of 75.3%(71.5 to 79.0) at 10 years and 60.5%(54.5 to 67.8) at 15 years compared to patients in whom the VSD was closed. There was no difference in the late survival for the groups in whom the VSD was closed at the primary operation or at a subsequent procedure(figure 5a). This is summarised in figure 5b where all patients who achieved VSD closure are grouped together verses those that have the VSD left open. This shows a clear survival benefit in those patients in whom the VSD is closed, with a 10 year survival of 93.0% and 15 year survival of 91.0%(p=0.003).

On multivariate analysis of risk factors(table 3), Group C anatomy had the greatest hazard for late mortality at 2.76. Cases suitable for single stage full correction carried the lowest hazard for late survival. The use of an AP window/Melbourne Shunt carried a slightly greater hazard (HR 1.46) than those undergoing single stage repair. In analysis of the number of MAPCAs that had to be recruited, the need to recruit ≥4 MAPCAs was associated with increased risk(HR 1.6) compared to those in whom ≤2 MAPCAs had to be recruited.

Discussion

This study has focused on a practical classification of patients according to the nature of their pulmonary blood supply – from native PAs, from MAPCAs or from a mixture of the two, recognizing that some areas of the lung have 'dual supply' from a MAPCA that feeds into a native PA system. Just under one half of the patients have a combination of native PAs and MAPCAs, with about one quarter having native vessels only (dual supplied by MAPCAs). The remaining cases (about one quarter) have absent native vessels and the pulmonary blood supply is exclusively from MAPCAs. Our philosophy is that unifocalisation should utilize both PAs and MAPCAs and can be achieved in close to 90% of all patients regardless of the classification, with very low early mortality. However, the latter group tend to have overall poorer vasculature and poorer long-term survival.

Although different strategies have been proposed around the world, common themes of early unifocalisation are increasingly favoured and the results of this series suggest that excellent outcomes can be achieved with a strategy of maximal recruitment of pulmonary vasculature and the establishment of RV-PA continuity. The use of using a limiting RV-PA conduit and leaving the VSD open is a successful means of managing the borderline cases. This study shows, in keeping with the Stanford group, that unifocalisation can be achieved in the majority of patients [13,14]. Those in whom this cannot be achieved are the worst end of the spectrum with poor vasculature and progressive cyanosis - probably 10-15% of all patients will fall into this group [9,13].
Earlier assessment and unifocalisation has been strongly advocated by the Stanford group [16] and is supported by this study. The median ages of the patients in our study was older than in the Stanford series (partly skewed by the proportion of much older children referred from outside our centre), but is steadily reducing and we would advocate early assessment and unifocalisation at 6-9 months wherever possible.

Careful assessment of the pulmonary vasculature at an early stage is paramount to the success of this strategy. Areas of the lung with unprotected high flow can develop pulmonary vascular disease, whereas other areas can be supplied by MAPCAs in which the proximal course is progressively stenosed (or even occluded). Early recruitment secures antegrade flow into the vascular bed and promotes growth.

This study supports the 'recruitment' philosophy of incorporating both native PAs and the MAPCAs into unifocalisation to achieve best outcomes. Some authors have favoured an alternative approach to focus on the native PA vessels only, excluding (and ligating) MAPCAs wherever possible, which is referred to as a 'rehabilitation strategy' [6,7]. Clearly, such a strategy is not feasible in the 15-20% of patients who have complete absence of native PA vessels(Group C) and, furthermore, we have shown that even in patients with a native PA system, some areas of the lung may have sole supply from MAPCAs that should be recruited. 'Rehabilitation alone' approaches report an ability to achieve repair in 60-73%[6,7,18], compared to 80% in our series and close to 90% in the Stanford series with outstanding results and low RV pressures[13,15,16]. Thus, although there is no doubt that the overall quality of native PAs is generally better than that of MAPCAs, the importance of MAPCA recruitment is crucial to success. Furthermore, the series that utilize native PAs alone report early mortality of 10% and more than half the patients had an RV pressure of >50% systemic at completion.

The intrinsic superiority of utilizing native PAs is supported by the finding that the long-term outcomes of Group A and B in this study were better than those of Group C. Nevertheless, there was no difference in early outcomes between all groups and the late survival of 80% was still achieved at 10 years in Group C, which have traditionally been the most challenging group to manage. We utilized the Melbourne shunt in about one third of patients in Group A and B. None of these patients were felt to be suitable for unifocalisation at initial presentation, yet the outcomes ultimately achieved for this group were the same as those who underwent single stage repair. Although the shunt was not necessary in the majority of patients, it is an invaluable interim step in the particular group of patients with small native PAs that have good distribution to the lungs. Nevertheless, it was important to note that whilst recruitment of additional MAPCAs was reduced, it remained an essential part of repair even the patients who responded well to the Melbourne shunt (mean of 1.8 MAPCAs per patient). This is the clear benefit of the 'rehabilitation' strategy and the results of this study suggest that best outcomes are achieved by combining the advantages of both rehabilitation and recruitment into a combined approach.

We have maintained a degree of flexibility over whether or not to close the VSD at the time of unifocalisation. Many authors describe the use of intra-operative flow studies to be a successful discriminator for VSD closure, calculating $3 l.min^{-1}.m^{-2}$ and accepting pressures of ≤25mmHg (Stanford[14]) or a protocol of $2.5 l.min^{-1}.m^{-2}$ with pressures of ≤30mmHg (Toronto[18]) and both groups have reported excellent results. We prefer to make an assessment based on the quality of the vasculature at pre-operative imaging and use the criterion of aiming to recruit ≥15/20 broncho-pulmonary segments. We feel that this works well with our philosophy of leaving the VSD open and placing a limiting (restrictive) RV-PA conduit in cases who fail to meet this threshold – other authors prefer a central shunt into the unifocalised vessels in this situation. The benefit of an RV-PA conduit is that it will be

delivering predominantly desaturated blood into the lungs and provide pulsatile flow - which provides optimal oxygen-delivery: flow ratio and a good stimulus for growth. The RV-PA conduit also allows the surgeon more flexibility, as it can be externally clipped or released to balance flow at completion of surgery, and provides good access for subsequent catheterization. Intra-operative flow studies can be difficult to perform accurately in our experience and borderline values make decision-making difficult. An important finding to support this approach is that delaying VSD closure does not impair long-term outcomes, with similar long-term survival for all cases who achieve complete repair, whether this is in a single stage or at a subsequent procedure. The overall approach to assessment and management is summarised in supplementary figure 2.

The patients in whom the VSD can never be closed are, by definition, those with poorer quality pulmonary vasculature and we feel these are more safely managed in this manner. The use of a restrictive RV-PA conduit provides a balanced circulation and avoids the RV being exposed to supra-systemic pressures. This arrangement can allow for a good quality of life in this more challenging group of patients.

In conclusion, a combined approach of rehabilitation and recruitment is recommended. Preliminary central shunts improve native PA growth but do not preclude the need to recruit MAPCAs. Patients with absent native PAs achieve good early outcomes but are at risk of decreased late survival. Our goal is always early unifocalisation, but it is safe to leave the VSD open and use a limiting RV-PA conduit as a valuable interim measure. Borderline patients can undergo subsequent complete repair with long term outcomes that are similar to those undergoing primary repair.

Limitations of the Study: The study focuses on unifocalisation and so contains only limited information on the small group in whom unifocalisation could never be achieved – this group of patients have the worst quality vasculature and much more guarded outcomes. Also, almost 20% of patients had been referred from outside institutions and so did not have a uniform approach from birth – often being much older at initial assessment. The study does not include uniform measurement of RV:LV pressure ratios at complete repair as these were not available for all patients. The long time period of the study cannot exclude an era effect, although no difference in outcomes by era could be demonstrated.

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Figures:

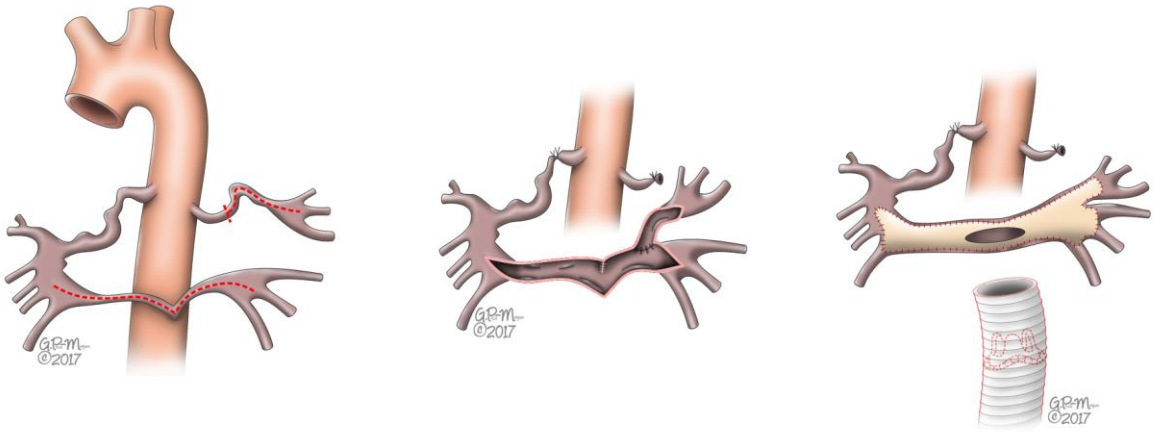


Figure 1. Unifocalization of a case with a combination of native pulmonary arteries (supplied by a single MAPCA, dual supply) and one area of the lung supplied by a MAPCA alone (left upper lobe). The MAPCA is recruited into the reconstructed native pulmonary arteries which are then connected to the right ventricle with a valved Dacron conduit.

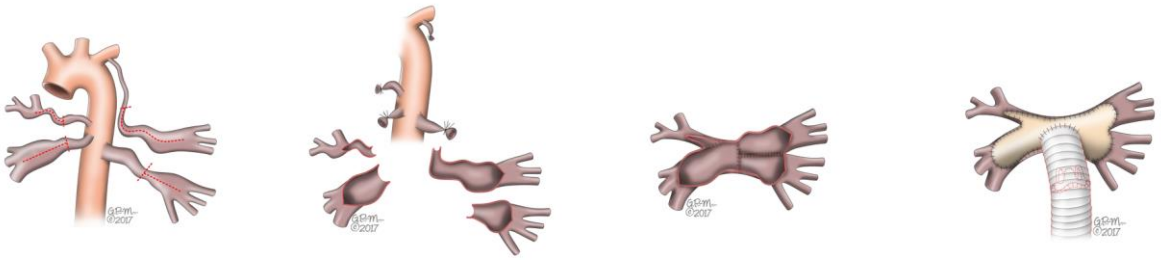


Figure 2. Unifocalisation in a case with four large MAPCAs but absent native central pulmonary arteries. The MAPCAs are disconnected from their origins, mobilized and brought together across the midline to create a platform. This confluence of vessels is then patched and connected to the right ventricle with a valved Dacron conduit.

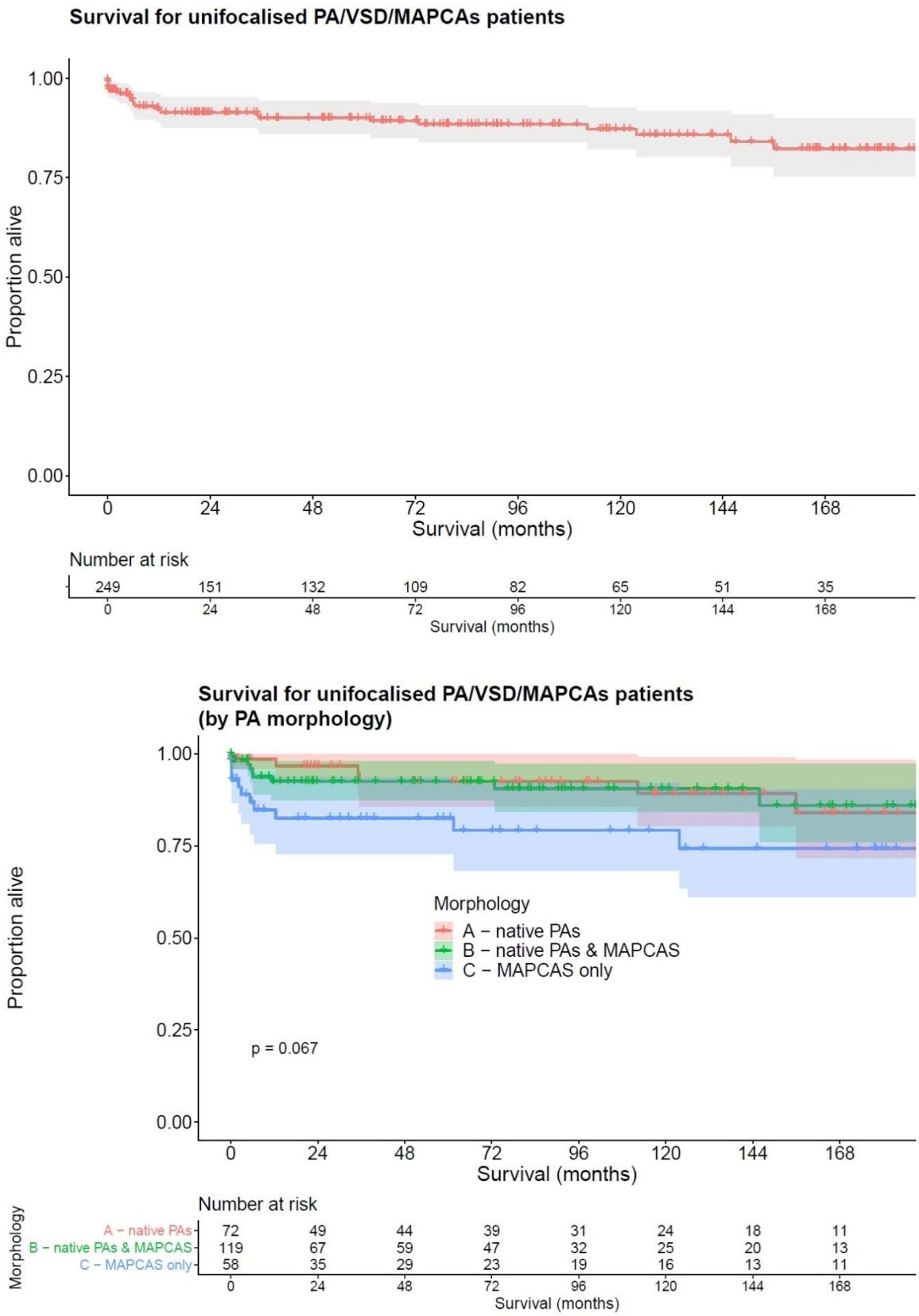


Figure 3. Kaplan-Meier Plot showing actuarial survival of 249 patients undergoing unifocalization of pulmonary atresia with VSD and MAPCAs. (a) Entire Population, (b) Survial by group according to pulmonary artery morphology [from Barron et al. 11].

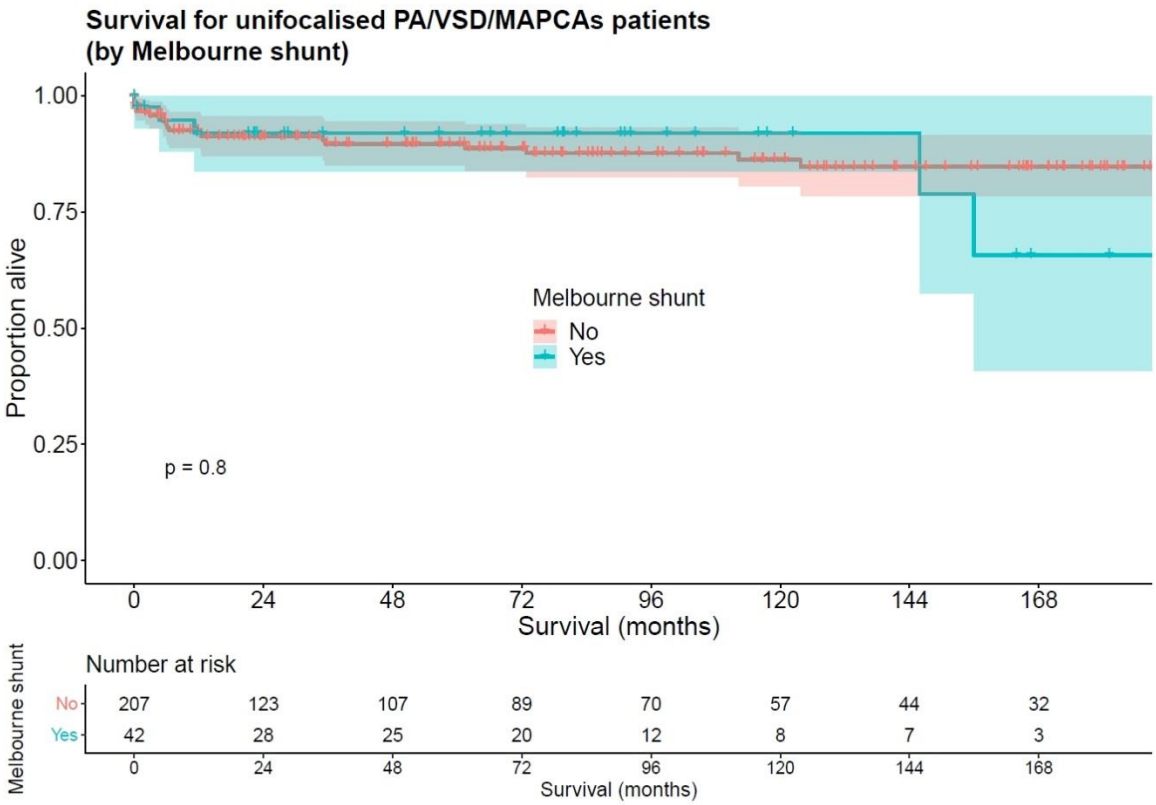


Figure 4. Kaplan-Meier survival curve according to use of a 'Melbourne' central shunt prior to complete repair.

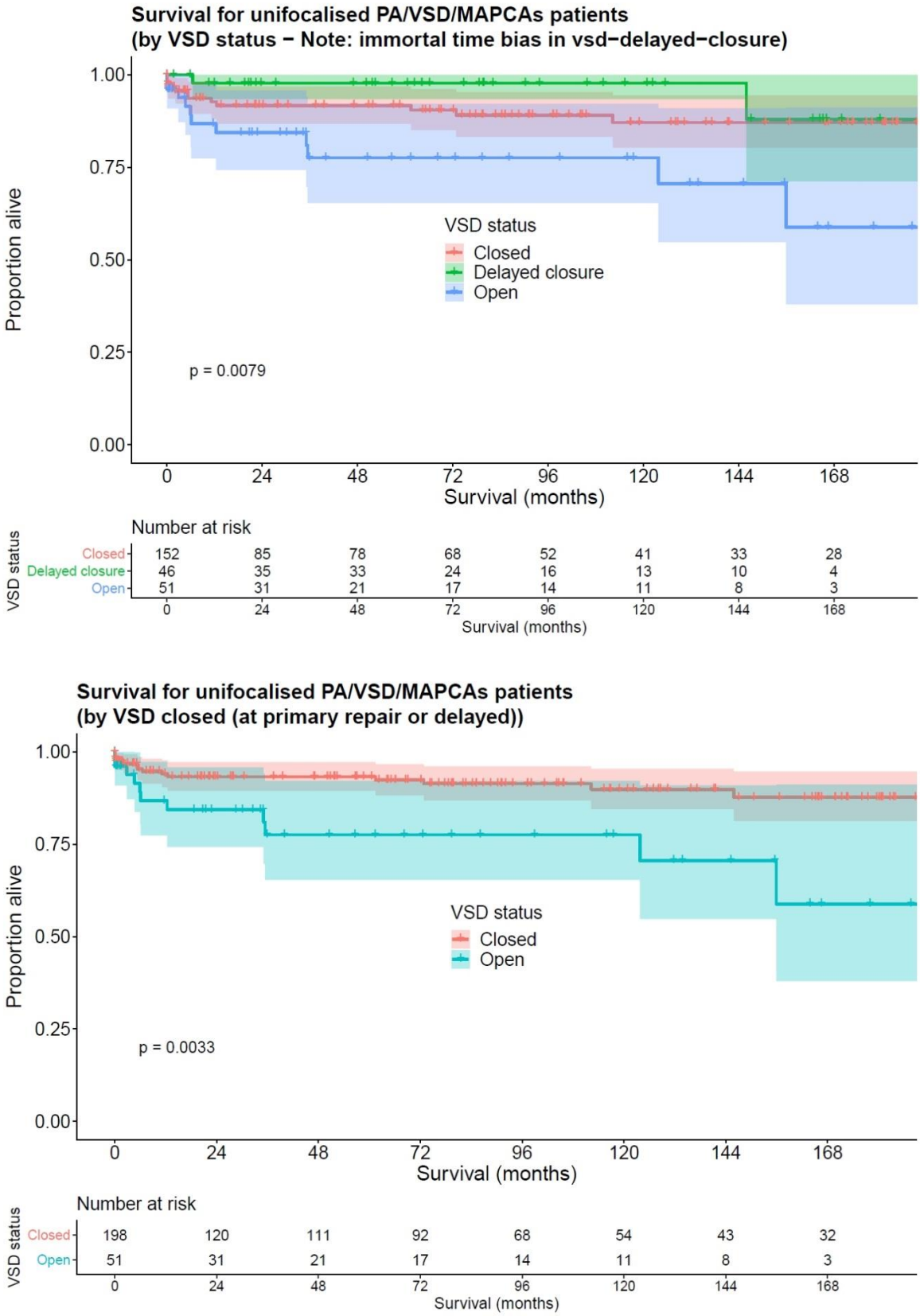
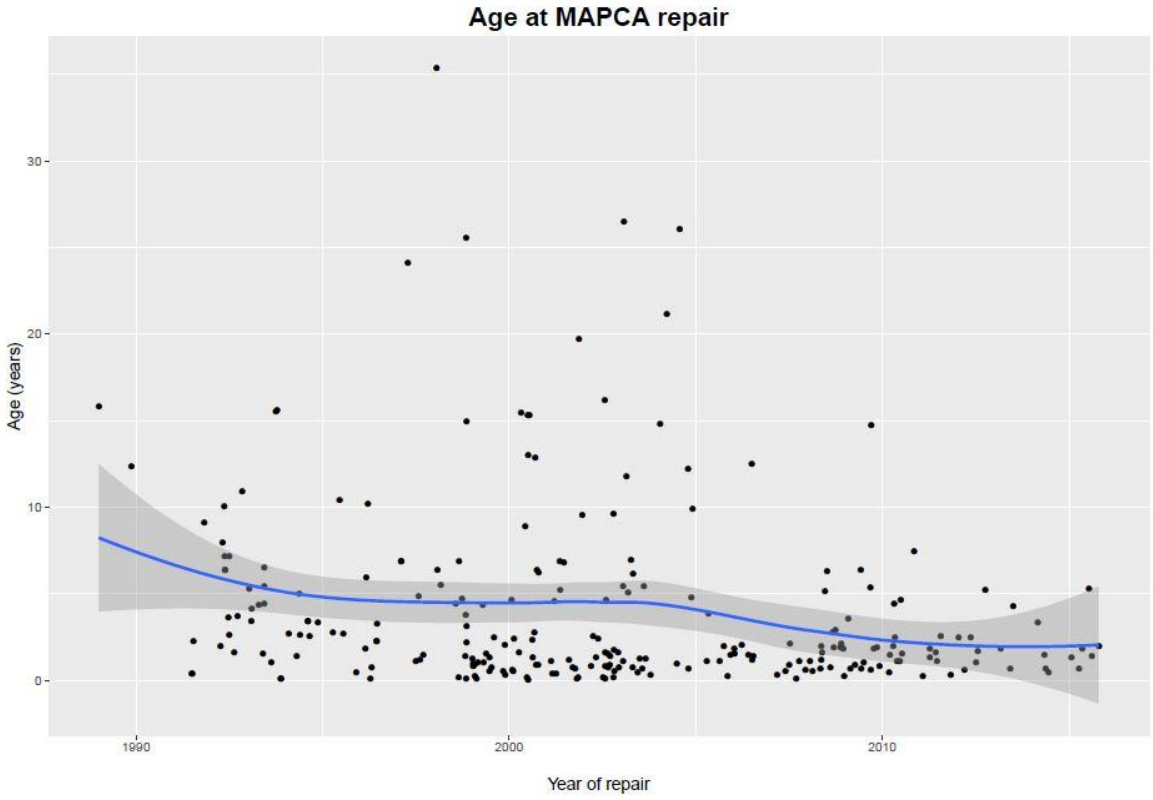
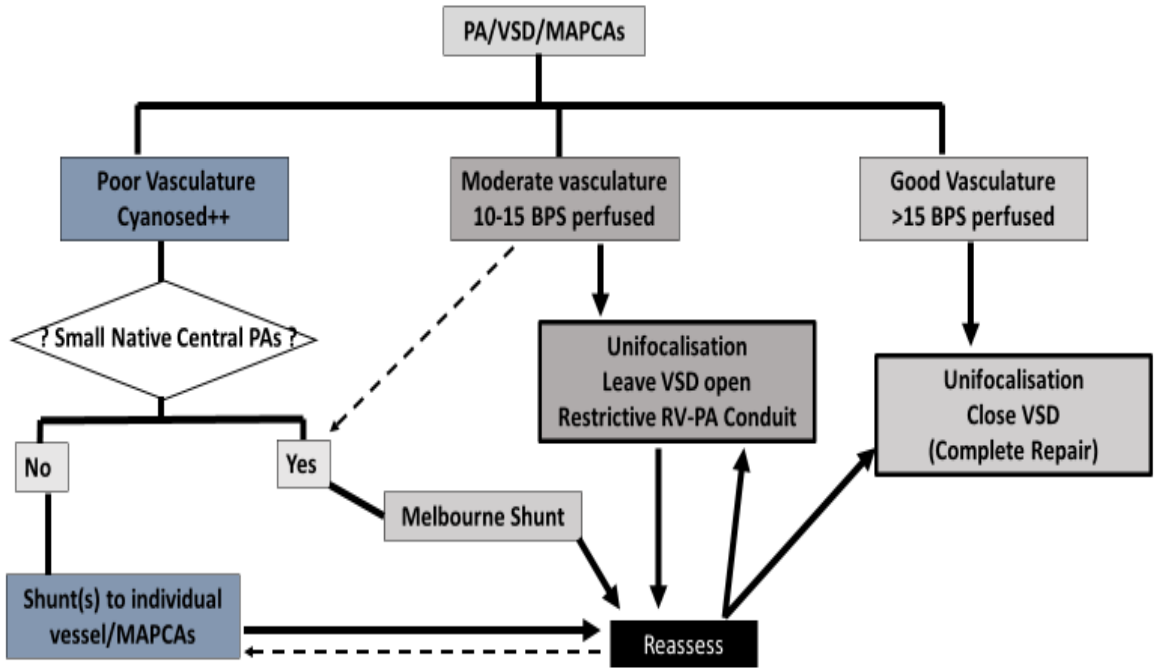


Figure 5. Kaplan-Meier survival curves according to timing of VSD closure in PA/VSD/MAPCAs. (a) Survival in groups according to those in whom VSD was closed at initial surgery, at subsequent surgery or never been closed. (b) Survival in groups according to whether the VSD left open or closed (either at initial or at subsequent surgery) [from Barron et al. 11]



Supplementary Figure 1: LOESS (Locally Estimated Scatterplot Smoother) plot showing variation in age at repair over the time period of the study



Supplementary Figure 2: Summary of management strategies for patients with PA/VSD/MAPCAs

Table 1. Demographics of patients undergoing unifocalisation (n=249).

	Overall (n=249)	Native PAs only (Gp A, n=72)	Native PAs + MAPCAs (Gp B, n=119)	Any native PAs (Gps A+B, n=191)	MAPCAs only (Gp C, n=58)	p value (A/B/C)
Age, months(median IQR)	23 (11-61)	26 (16 to 62)	21 (11 to 65)	24 (13 to 64)	18 (9 to 39)	0.12
Male, n (%)	109 (43.8)	34 (47.2)	48 (40.3)	82 (42.9)	27 (46.6)	0.58
DiGeorge, n (%)	72 (28.9)	16 (22.2)	34 (28.6)	50 (26.2)	22 (37.9)	0.14
Single-stage repair, n (%)	111 (44.6)	22 (30.6)	56 (47.1)	78 (40.8)	33 (56.9)	0.01
MAPCAs (median (Q1-Q3)	3 (2 to 4)	3 (2 to 3)	3 (3 to 4)	3 (2 to 4)	3 (2 to 4)	-
MAPCAs (mean, SD)	3.11 (1.25)	2.46 (1.09)	3.39 (1.23)	3.04 (1.26)	3.34 (1.19)	<0.001
Delayed VSD closure, n(%)	94 (37.8)	21 (29.2)	51 (42.8)	72 (37.6)	22 (37.9)	0.13
VSD left open, n (%)	51 (20.5)	13 (18.1)	26 (21.8)	39 (20.4)	12 (20.7)	0.82
30-day mortality, n (%)	7 (2.8)	1 (1.4)	2 (1.7)	3 (1.6)	4 (6.9)	0.10

* Change in median age by era, divided into quartiles (median,Q1-Q3): q1 44.3 (30.1-83.5) months
q2 24.2 (9.7-71.3) months
q3 18.0 (9.1-50,6) months
q4 18.1 (8.7-26.2) months

Table 2. Use of central shunt and the number and destiny of MAPCAs by group.

Group	n	Initial central shunt	Total MAPCAs No./case	MAPCAs recruited no./case	MAPCAs ligated no./case
Native PAs only (A)	72 (28.9%)	11/72 (15.3%)	180 (2.5±1.1)	0	142 (2.7±1.2)
Native PAs + MAPCAs (B)	119 (47.8%)	45/119 (37.8%)	406 (3.4±1.2)	286 (2.4±1.3)	109 (1.9±1.0)
MAPCAs only (C)	58 (23.4%)	0	200 (3.4±1.2)	188 (3.3±1.2)	13 (0.2±0.6)

MAPCAs, major aortopulmonary collateral arteries; PAs, pulmonary arteries.

Table 3: Hazard ratios for survival on multivariate analysis

Factor	Hazard ratio	Lower 0.95 CI	Upper 0.95 CI
Number of MAPCAs (4 compared to 2)	1.62	0.89	2.96
Group A-Native : Group B-Native & MAPCAs	1.00	0.34	2.94
Group C-MAPCAs only :Group B-Native & MAPCAs	2.76	1.08	7.08
Melbourne shunt - yes:no	1.46	0.47	4.53
One stage repair - yes:no	0.45	0.18	1.11

Wald statistic for overall model 11.5 with 5 degrees of freedom, P = 0.04.