Subdiaphragmatic venous hemodynamics in patients with biventricular and Fontan circulation after diaphragm plication

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Objective: Diaphragm paralysis owing to phrenic nerve injury can result in significant morbidity in children undergoing surgical management of congenital cardiac defects. Diaphragm plication is the accepted therapy for diaphragm paralysis. We have investigated subdiaphragmatic venous hemodynamics in patients with biventricular and Fontan circulation after diaphragm plication.

Methods: Doppler ultrasound was used to evaluate flows in the hepatic vein, portal vein, and subhepatic inferior vena cava under respiratory monitoring and with a tilt table. Twenty-nine patients with biventricular circulation were studied: 19 with normal diaphragms and 10 after diaphragm plication. Twenty-eight patients with total cavopulmonary connections after the Fontan procedure were also studied: 19 with normal diaphragms and 9 with plicated diaphragms. Inspiratory/expiratory flow ratios in supine and upright positions were calculated to investigate respiratory effects, and upright/supine flow ratios were calculated to assess gravity effects.

Results: In patients with biventricular circulation and normal diaphragms, hepatic venous flow was augmented by inspiration; this effect was reduced in patients with a plicated diaphragm (upright inspiratory/expiratory flow ratios: 2.4 vs 1.4, respectively; $P = .01$). Portal venous flow was higher during expiration; this effect was lost in patients with a plicated diaphragm (supine inspiratory/expiratory flow ratios: 0.8 and 1.0; $P < .05$). In Fontan patients with normal diaphragms, hepatic venous flow depended heavily on inspiration. This effect was blunted in patients with a plicated diaphragm (supine inspiratory/expiratory flow ratios: 3.2 vs 2.3; $P < .05$). Expiratory augmentation of portal flow was absent in Fontan patients with normal diaphragms and reversed in patients a plicated diaphragm (supine inspiratory/expiratory flow ratios: 1.0 vs 1.6; $P = .02$). Gravity reduced Fontan portal venous flow; having a plicated diaphragm did not alter this effect (upright/supine flow ratios: 0.7 vs 0.7).

Conclusions: In patients with biventricular and those with Fontan circulation with a paralyzed diaphragm, plication does not completely restore normal subdiaphragmatic venous hemodynamics. In Fontan patients with a plicated diaphragm, important inspiration-derived hepatic venous flow is suppressed, and portal venous flow loses its normal expiratory augmentation. These flow dynamics share similarities with those observed in patients with failing Fontan circulation. This suboptimal splanchnic circulation may contribute to early problems of prolonged pleural effusions and ascites and potentially may promote late Fontan failure. Phrenic nerve injury should consequently be avoided at all costs before or at the time of the Fontan operation.

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Respiration and gravity constantly exert important and, at times, negative influences on venous return dynamics. Classic physiologists, such as Brecher,¹ Guyton,² and Moreno and Burchell,³ have demonstrated that the biventricular heart compensates for these influences so that they are normally unnoticed. Fontan circulation places additional stress on venous return, especially in the subdiaphragmatic region where hydrostatic pressure and interposition of the liver pose further challenges to the passive venous hemodynamics.⁴ In several studies focusing on subdiaphragmatic venous hemodynamics, we⁵⁻⁷ have demonstrated that the splanchnic venous circulation is a particularly vulnerable part of the Fontan circulation. In patients with the Fontan circulation, hepatic venous flow is primarily driven by inspiration.⁷ A loss of hepatic–portal circulatory autoregulation results in a portal venous system that is unprotected from elevated hepatic venous pressure and subject to exaggerated gravitational stress.⁵ These anomalies are amplified in “failing” Fontans or in patients with elevated Fontan pressures.⁵ On the basis of these observations, we postulated that patients who have had the Fontan operation are likely to be highly susceptible to disturbances of respiratory mechanics, such as diaphragm paralysis owing to phrenic nerve injury, and thus may benefit from early diaphragm plication.⁵

Two retrospective case-control analyses of patients with Fontan circulation have shown that diaphragm paralysis significantly increases postoperative morbidity, including prolonged pleural effusions, longer hospital stay, chronic ascites, and higher rate of hospital readmission.^{8,9} Both studies suggested that early diaphragm plication would improve and reoptimize Fontan flow dynamics and potentially avoid late complications.

In children with biventricular circulation, early surgical plication has been recognized to limit the morbidity associated with diaphragm paralysis and its resultant respiratory disturbance.¹⁰⁻¹² However, it remains unknown whether diaphragm plication restores venous flow dynamics to normal. The purpose of this study is to examine whether the effects of respiration and gravity on subdiaphragmatic flow dynamics are normalized in patients with biventricular and Fontan circulation after diaphragm plication for phrenic nerve palsy.

Patients and Methods

Study Groups

Twenty-nine patients with biventricular circulation were studied: 10 had undergone surgical diaphragm plication for diaphragm paralysis (group BV-DP). They were in self-reported New York Heart Association (NYHA) functional class I or II (9:1, respectively) and were 7 to 17 years of age (mean 11 ± 3 years). Nine BV-DP patients had undergone previous surgery: 2 tetralogy of Fallot repairs, 1 arterial and

Abbreviations and Acronyms

IVC	= inferior vena cava
NYHA	= New York Heart Association
Q _{ex}	= expiratory flow rate
Q _{in}	= inspiratory flow rate
Q _{sup}	= flow rate in the supine position
Q _{up}	= flow rate in the upright position
TCPC	= total cavopulmonary connection

1 atrial switch operation for transposition of the great arteries, 1 interrupted aortic arch repair, 1 open pulmonary valvotomy for pulmonary stenosis, 1 orthotopic heart transplant, 1 atrioventricular septal defect repair, and 1 mediastinal teratoma resection. One BV-DP patient with no structural heart defect required right hemidiaphragm plication for phrenic nerve palsy as a complication of pneumonia/emphysema. Nine had plication of a unilateral diaphragm (6 left, 3 right), and 1 patient underwent bilateral diaphragm plications. Nineteen age- and sex-matched normal volunteers were studied as controls for the biventricular analysis (group BV).

Twenty-eight patients were studied 1 to 13 years (mean 7 ± 4 years) after a total cavopulmonary connection (TCPC: lateral tunnel or extracardiac conduit). Nine had previously undergone a unilateral diaphragm plication (group TCPC-DP) for diaphragm paralysis (8 right and 1 left); 5 were in NYHA class I, 1 in class II, and 3 in class III. The remaining 19 TCPC patients with no diaphragm plication were in self-reported NYHA functional class I (group TCPC); none had clinical signs of congestive heart

TABLE 1. Gravity effects on flows in biventricular and Fontan patients

Biventricular patients	Gravity effect Q _{up} /Q _{sup}	Fontan patients	Gravity effect Q _{up} /Q _{sup}
Hepatic vein			
BV	0.8 ± 0.3	TCPC	0.6 ± 0.3
BV-DP	0.6 ± 0.3	TCPC-DP	0.8 ± 0.3
P value	.14	P value	.2
Portal vein			
BV	0.8 ± 0.5	TCPC	0.7 ± 0.3
BV-DP	0.9 ± 0.3	TCPC-DP	0.7 ± 0.2
P value	.5	P value	.8
IVC			
BV	1.0 ± 0.5	TCPC	0.7 ± 0.2
BV-DP	0.9 ± 0.7	TCPC-DP	0.8 ± 0.2
P value	.14	P value	.3

BV, Biventricular subjects; BV-DP, biventricular patients with diaphragm plication; TCPC, total cavopulmonary connection patients; TCPC-DP, total cavopulmonary connection patients with diaphragm plication; Q_{up}, net flow in upright position; Q_{sup}, net flow in supine position; IVC, subhepatic inferior vena cava. P values by *t* tests.

TABLE 2. Respiratory effects on flows in biventricular patients

	Supine respiratory effect (Qin/Qex)sup	Upright respiratory effect (Qin/Qex)up	Intragroup, supine vs upright, P value
Hepatic vein			
BV	17 ± 0.5	2.4 ± 1.2	.01
BV-DP	2.0 ± 0.9	1.4 ± 0.3	.08
Intergroup P value	.3	.01	
Portal vein			
BV	0.8 ± 0.3	0.8 ± 0.3	.6
BV-DP	1.0 ± 0.4	0.9 ± 0.3	.09
Intergroup P value	<.05	.3	
IVC			
BV	1.2 ± 0.3	1.4 ± 0.4	.24
BV-DP	1.1 ± 0.3	1.3 ± 0.3	.15
Intergroup P value	.3	.7	

BV, Biventricular subjects; BV-DP, biventricular patients with diaphragm plication; Qup, net flow in upright position; Qsup, net flow in supine position; IVC, subhepatic inferior vena cava. P values by *t* tests.

failure, arrhythmia, major pulmonary arteriovenous malformations, protein-losing enteropathy, or other known complications of the Fontan circulation. Six patients in the TCPC-DP group had a fenestrated inferior pathway and 5 in the TCPC group.

For both BV-DP and TCPC-DP groups, the diagnosis of diaphragmatic paralysis was confirmed by either ultrasonographic or fluoroscopic interrogation in the immediate postoperative period or before hospital discharge. Diaphragm plications were used before discharge or to assist mechanical ventilatory weaning. In all cases, the surgical method used involved a limited lateral thoracotomy on the affected side and the diaphragm was plicated by the standard central pleating technique. There was no formal interval study of diaphragm function.

All subjects underwent hepatic venous, portal venous, and infrahepatic inferior vena caval (IVC) Doppler ultrasonographic interrogation under simultaneous dynamic respiratory and electrocardiographic monitoring. A tilt table was used to allow measurements in the supine and upright (85°-90° from horizontal plane) positions. In addition, ultrasonographic examination of bilateral diaphragmatic excursion was performed in all subjects to document diaphragm function. The study protocol was approved by the hospital research ethics committee, and informed consent was obtained for all subjects.

TABLE 3. Respiratory effects of flows on Fontan patients

	Supine respiratory effect (Qin/Qex)sup	Upright respiratory effect (Qin/Qex)up	Intragroup, supine vs upright, P value
Hepatic vein			
TCPC	3.2 ± 1.3	2.5 ± 1.0	.03
TCPC-DP	2.3 ± 0.8	1.7 ± 0.6	.06
Intergroup P value	<.05	.04	
Portal vein			
TCPC	1.0 ± 0.3	1.0 ± 0.2	.2
TCPC-DP	1.6 ± 0.9	1.7 ± 0.6	.2
Intergroup P value	.02	.04	
IVC			
TCPC	1.6 ± 1.7	1.9 ± 2.9	.3
TCPC-DP	1.4 ± 0.2	1.7 ± 0.6	.2
Intergroup P value	.7	.8	

TCPC, Total cavopulmonary connection patients; TCPC-DP, total cavopulmonary connection patients with diaphragm plication; Qin, inspiratory flow rate; Qex, expiratory flow rate; sup, supine position; up, upright position; IVC, subhepatic inferior vena cava. P values by *t* tests.

Doppler Ultrasound Recordings

The methodology, mathematical background, and flow rate calculations used in this study were described in detail previously.⁵⁻⁷ In brief, pulsed-wave Doppler recordings in the hepatic vein, portal vein, and IVC were made with each subject breathing quietly in the supine and then the upright position. Recordings were made in the left or middle hepatic vein (approximately 1 cm proximal to the junction with the IVC) and the infrahepatic IVC (1-2 cm proximal to the junction with the hepatic vein). The portal flow signal was obtained in the main portal trunk before its division into the right and left branches, following previously published protocols.¹³ Volumetric flow rates in hepatic vein, portal vein, and IVC were calculated from velocity time integrals and the measured vessel diameters from the Doppler recording.

Gravity Effect

The effect of gravity on net flow rate was evaluated. Net flow rate was defined as the absolute total flow during a complete respiratory cycle obtained by subtracting the retrograde velocity time integral from the antegrade velocity time integral. The effect of gravity on flow rate was represented as the ratio of flow rate in the upright position over that in the supine position, Qup/Qsup. A ratio of less than 1 signifies reduced flow in the upright position.

Respiratory Effect

The Doppler signal was evaluated during inspiration, during expiration, and throughout a complete respiratory cycle.⁵⁻⁷ Flow rates during the inspiratory phase, Q_{in} , of the respiratory cycle were determined, as well as during the expiratory phase, Q_{ex} . The effect of respiration on flow was expressed as a ratio of Q_{in}/Q_{ex} and was measured in both supine and upright positions for all 3 venous regions of interest. When Q_{in} is higher than Q_{ex} , Q_{in}/Q_{ex} ratio is greater than 1, and vice versa.

Statistical Analysis

All data are expressed as mean $\pm$ standard deviation. Comparisons of (1) normal against biventricular patients with plicated diaphragms (BV vs BV-DP) and (2) TCPC patients against those with plicated diaphragms (TCPC vs TCPC-DP) were performed with 2-tailed t tests. To evaluate the influence of upright posture on Q_{in}/Q_{ex} , we conducted intragroup examinations of Q_{in}/Q_{ex} in the supine versus Q_{in}/Q_{ex} in the upright position using paired t tests.

Results

Study Group Characteristics

There were no significant differences in age and male/female distribution between BV-DP and BV subjects. Among TCPC patients, those with a plicated diaphragm were slightly younger than those without (11 ± 3 years TCPC-DP vs 15 ± 5 years TCPC; $P = .04$) and all were male (9:0 TCPC-DP vs 14:5 TCPC; male/female). In addition, a greater proportion had undergone an extracardiac conduit versus lateral tunnel TCPC (5:4 TCPC-DP vs 2:17 TCPC; extracardiac conduit/lateral tunnel). Similar to our previous study,⁷ there were no quantitative differences between the extracardiac conduit and lateral tunnel TCPC patients within each study group, so their data are presented together.

There were no differences in room air oxygen saturation between (1) BV-DP and BV subjects ($98\% \pm 1\%$, vs $97\% \pm 2\%$) and between (2) TCPC-DP and TCPC patients ($89\% \pm 5\%$ vs $89\% \pm 4\%$).

All BV and TCPC patients had normal bilateral diaphragm excursion under ultrasonographic interrogation. Patients with a previous diaphragm plication all had severely limited or absent diaphragm mobility on the affected side(s) throughout the respiratory cycle. None had paradoxical diaphragm movement.

Flow Dynamics

Gravity effects on flow: Q_{up}/Q_{sup} . The results of the Doppler flow rate calculations for gravity effects on flow are summarized in Table 1. In the BV patients, gravity reduced hepatic and portal venous flows by 20% and had no significant influence on IVC flow. Diaphragm plication did not

alter these effects significantly. In TCPC patients, gravity reduced flows in the hepatic and pulmonary veins and in the IVC. TCPC-DP patients showed similar effects (Table 1).

Respiratory effects on flow: Q_{in}/Q_{ex} . Tables 2 and 3 present the Doppler calculations for respiratory effects on flow. Respiratory effects in the supine and upright positions are compared between biventricular subjects with or without a plicated diaphragm (Table 2) and between TCPC patients with or without a plicated diaphragm (Table 3).

BIVENTRICULAR PATIENTS (TABLE 2). Hepatic venous flow was higher during inspiration in both BV and BV-DP patients. In the supine position, this effect was similar in the 2 groups. In the upright position, BV patients exhibited higher inspiratory flow augmentation than BV-DP patients (Figure 1). In BV patients, portal venous flow was higher during the expiratory phase of the respiratory cycle. This effect was lost in BV-DP patients, in whom inspiratory flow was equal to expiratory flow in the supine position (Figure 2). Augmentation of IVC flow during inspiration was similar in BV and BV-DP patients.

TCPC PATIENTS (TABLE 3). Hepatic venous flow in TCPC patients occurred primarily during the inspiratory phase of the respiratory cycle. In both the supine and upright positions, this mechanism was significantly blunted in TCPC patients with a plicated diaphragm (Figure 3).

The expiratory augmentation of portal venous flow seen in BV patients was absent in TCPC patients. In TCPC-DP patients, the portal venous flow pattern was the reverse of normal, with higher flow during inspiration in both the supine and upright positions ($Q_{in}/Q_{ex} = 1.6 \pm 0.9$ supine and 1.2 ± 0.3 upright) (Figure 2). IVC flow was augmented by inspiration in TCPC patients, an effect that was maintained in TCPC-DP patients.

Coupled gravity and respiratory effects: Upright (Q_{in}/Q_{ex}) versus supine (Q_{in}/Q_{ex}) biventricular patients (Table 2). In BV patients, upright posture enhanced inspiratory hepatic venous flow augmentation (Q_{in}/Q_{ex} : 1.7 ± 0.5 supine vs 2.4 ± 1.2 upright) (Figure 4). In BV-DP patients, this accentuation of the respiratory effect by the upright posture is lost (Q_{in}/Q_{ex} : 2.0 ± 0.9 supine vs 1.4 ± 0.3 upright) (Figure 1). In the portal vein, upright posture appeared to partially restore expiratory augmentation toward normal (Q_{in}/Q_{ex} : 1.0 ± 0.4 vs 0.9 ± 0.3), but this did not reach statistical significance ($P = .09$). Postural change did not affect the respiratory effect on IVC flow in either BV or BV-DP patients.

TCPC PATIENTS (TABLE 3). In both TCPC and TCPC-DP patients, upright posture resulted in a suppression of hepatic venous inspiratory drive (Figures 3 and 5). This effect was similar to that in BV-DP patients. Posture change did not affect the respiratory effect on portal venous or IVC flow in either group of TCPC patients.

Figure 1. Respiratory effect on hepatic venous flow in biven-tricular patients (BV) and biven-tricular patients with diaphragm plication (BV-DP). The data ob-tained in supine and upright po-sitions are depicted. Q_{in} , Inspiratory flow rate; Q_{ex} , expiratory flow rate. P values by un-paired and paired t tests as appropriate.

Discussion

The diaphragm is the most important inspiratory muscle.¹⁴ Unilateral diaphragm paralysis reduces inspiratory muscle force. Combined with its paradoxical upward displacement,

this leads to inability of the patient to inspire to total lung capacity and substantially decreases pulmonary function.^{15,16} By eliminating paradoxical movement and increasing kinetics of the unaffected hemidiaphragm, plication of the para-

Figure 2. Respiratory effect on supine portal venous flow in biventricular and Fontan (TCPC) patients with and without a diaphragm plication. BV, Biven-tricular subjects; BV-DP, biven-tricular patients with diaphragm plication; TCPC-DP, Fontan pa-tients with diaphragm plication; Q_{in} , inspiratory flow rate; Q_{ex} , expiratory flow rate. P values by unpaired t tests.

Figure 3. Respiratory effect on hepatic venous flow in Fontan patients (TCPC) and Fontan patients with diaphragm plication (TCPC-DP). *Qin*, Inspiratory flow rate; *Qex*, expiratory flow rate. *P* values by unpaired and paired *t* tests as appropriate.

lyzed diaphragm improves tidal volume and maximum breathing capacity. This is because stabilization of the paralyzed diaphragm improves the ability of the unaffected hemidiaphragm to act as a pressure generator and increases diaphragmatic contribution to breathing.¹⁷ However, studies have shown that diaphragm plication does not completely restore the impaired respiratory mechanics to normal.^{15,17}

Diaphragm paralysis owing to phrenic nerve injury has long been known to be a serious complication of cardiac surgery in children.^{10,11,18} The resulting respiratory insufficiency can lead to prolonged mechanical ventilation and its associated comorbidities: pulmonary infection, longer intensive care unit and hospital stay, and potentially higher mortality. Consequently, it has been recognized that early

Figure 4. Respiratory effect on hepatic venous flow in biventricular subjects (BV). Each *line* joins supine to upright values in a single patient. *P* value by paired *t* test. *Qin*, Inspiratory flow rate; *Qex*, expiratory flow rate.

Figure 5. Respiratory effect on hepatic venous flow in Fontan patients (TCPC). Each *line* joins supine to upright values in a single patient. *P* value by paired *t* test. *Qin*, Inspiratory flow rate; *Qex*, expiratory flow rate.

surgical plication can reverse some of these risks and prevent related morbidity.^{12,18,19} Subdiaphragmatic venous return, especially the portal–hepatic venous axis, is constantly affected by the dynamic interactions among the liver, diaphragm, and intrathoracic pressure changes. It remains unknown whether surgical plication of a paralyzed diaphragm restores the systemic venous flow dynamics.

This question is particularly relevant in patients undergoing the Fontan operation. The negative intrathoracic pressure generated by normal respiration is responsible for a majority of splanchnic venous drainage; hepatic venous flow during inspiration is more than 3 times that during expiration.⁷ Therefore, Fontan patients would be expected to poorly tolerate the impaired respiratory mechanics resulting from a paralyzed diaphragm, a maladaptation that is likely to be most evident within the hepatic–portal circulation. Unfortunately, perhaps owing to the necessity of multiple operations, up to 9% of Fontan patients have diaphragm paralysis as a result of inadvertent phrenic nerve injury during surgery.⁹ In 2 recent series, diaphragm paralysis increased the risk of early and midterm complications, including prolonged hospital stay, pleural effusions, readmission rates, and incidence of ascites.^{8,9} Although definitive conclusions could not be made, both articles reported anecdotal experience of improved outcomes and reversal of ascites with diaphragm plication. On the basis of these observations, the authors advocated heightened suspicion for diaphragm paralysis after a Fontan operation and early surgical plication once the diagnosis is made. However, the question remains of whether diaphragm plication can restore optimal Fontan hemodynamics.⁸

Patients With Biventricular Circulation

In a series of investigations, we⁵⁻⁷ have reported that respiration and gravity are two important factors affecting subdiaphragmatic venous flow in patients with normal and Fontan circulation. Normally, gravity and respiration are associated intimately in their influence on the subdiaphragmatic venous circulation. By adopting diaphragm plication as a proxy for a deranged respiratory mechanic, the current study established a clinical model that decouples respiratory and gravity influences and examined their effects individually and together.

The present investigation found that biventricular patients with a plicated diaphragm (group BV-DP) have altered venous flow dynamics. This is the first study of which we are aware that has reported this finding. Our data demonstrate that when diaphragm function is normal, the negative intrathoracic pressure created by inspiration augments hepatic venous return, and upright posture accentuates this phenomenon. Two synergistic mechanisms are responsible for this observed postural effect. First, in the supine position and during quiet tidal breathing, the lower rib cage behaves

as if it is driven by transabdominal rather than intrathoracic pressure.¹⁴ Thus, in the supine position, most breathing is abdominal; in the upright position, rib cage motion is greater.¹⁶ The consequence is that lung volume change is higher and the negative intrathoracic pressure generation is more pronounced in the upright position. Second, in the upright position, other accessory muscles are recruited to aid inspiration. For example, abdominal muscle contraction actively raises and stretches the diaphragm to maximize its caudal displacement and pressure generation during inspiration. This ventilatory mechanical advantage only operates in the upright position, where gravity aids passive diaphragmatic descent.¹⁴ Studies in normal subjects have shown that vital capacity drops by 20% in the supine position.¹⁴ This figure corresponds closely to the 29% loss of hepatic venous respiratory effect calculated from our data (BV hepatic venous Qin/Qex: 2.4 upright to 1.7 supine). In biventricular patients with a plicated diaphragm, augmentation of hepatic venous flow by the “respiratory pump” has lost this upright postural advantage.

Having a plicated diaphragm also alters the portal venous flow characteristics. As reported previously, normal portal venous flow decreases during inspiration, as the descending diaphragm compresses the compliant hepatic sinusoids and portal venules to displace portal inflow.^{3,5} The hepatic sinusoids are the site of both resistance and compliance in the portal–hepatic circulation, and normal portal flow is augmented during expiration.²⁰ The loss of expiratory portal flow augmentation in biventricular patients with a plicated diaphragm implies a decreased hepatic compressibility and reserve, a finding that is similar to our previous observation in Fontan patients.^{5,20-22}

Patients With Fontan Circulation

In patients with the Fontan circulation, pulmonary vascular resistance and systemic venous resistance are in series. This circulatory arrangement amplifies respiratory and gravitational modulations of venous return in Fontan patients.²³ We have previously demonstrated in TCPC patients that hepatic venous flow is primarily *driven* by inspiration. This phenomenon is observed whether the patient is well or in a failing state, is independent of Fontan pressure levels, and is enhanced by fenestration in the TCPC pathway.⁵⁻⁷ Our current findings demonstrate that the inspiratory drive of hepatic venous return in TCPC patients is significantly blunted after diaphragm plication, despite a greater proportion of TCPC-DP patients having a fenestrated pathway. Therefore, the present study not only confirms the importance of the “respiratory pump” in TCPC patients but also points out that altered respiratory mechanics, exemplified in patients with a plicated diaphragm, can suppress this major energy source for hepatic venous drainage. Such a deficit can potentially further impair a splanchnic physiology that

is already abnormal in Fontan patients. For example, the suppression of hepatic venous respiratory effect by upright posture is exacerbated in TCPC-DP patients (Qin/Qex: 2.3 supine vs 1.7 upright).

The consequences of suboptimal respiratory mechanics on the splanchnic circulation are also seen in the portal venous flow, which is vulnerable to upstream disturbances in the hepatic venous or central caval systems.^{21,24} Our data show that even in TCPC patients with functioning diaphragms, portal flow has lost its normal expiratory augmentation. Furthermore, in TCPC-DP patients with a plicated diaphragm, portal flow is reversed from normal, so that flow is higher during inspiration than during expiration. This is a phenomenon that we have previously observed in Fontan patients in poor functional status or with elevated Fontan pressures, and it is a reflection of increased hepatic congestion and decreased hepatic compliance and reserve.⁵ In such patients, congested hepatic sinusoids become dilated and are recruited into an open tube system, which allows portal flow to occur during the same phase of respiration as the hepatic venous flow.^{3,22,25} The fact that portal dynamics in TCPC patients with a plicated diaphragm are similar to those in patients with failing Fontan circulation suggests that, despite improving ventilatory mechanics, surgical plication does not completely restore splanchnic flow dynamics. Therefore, even with surgical plication, diaphragm paralysis is not completely compensated in TCPC patients and may increase the risk of late complications, such as ascites and protein-losing enteropathy, both of which have been linked to splanchnic venous congestion.²⁶

The initial research question of this study was to find out the impact of diaphragmatic paralysis in the Fontan circulation. Unfortunately, we could not answer this question because, similar to other groups,^{9,18} our institution adopted a proactive approach of performing early surgical plication in Fontan patients when a paralyzed diaphragm was diagnosed. Therefore, we do not have data from Fontan patients with a paralyzed diaphragm before plication. However, our data suggest that disturbances in ventilatory mechanics may have a more detrimental effect on the splanchnic venous return in Fontan patients than in biventricular patients. It is also evident that patients with a plicated diaphragm have some generalized defects in their splanchnic venous return that are present in either biventricular or Fontan physiology. In other words, even with a biventricular circulation, some of the splanchnic flow dynamics are abnormal and resemble those seen in Fontan patients.

The current study shed light on subdiaphragmatic venous flow anomalies that persist despite diaphragmatic plication, which is a consequence of phrenic nerve injury. Therefore, protection of the phrenic nerve before and during the Fontan operation is paramount. Because of its long course from the neck to the diaphragm, the phrenic nerve is susceptible to

inadvertent damage during operations for congenital cardiac disease owing to topical cold injury, traction injury resulting from tension, vena caval annulations, and direct trauma from electrocute dissection.^{11,27-29} The necessity of multiple reoperations in patients with single ventricle likely increases their risk of phrenic nerve injury.⁹ The left phrenic nerve is vulnerable during aortic arch reconstruction for the stage I Norwood operation or when a left modified Blalock-Taussig shunt is dissected before its closure. The right phrenic nerve is at risk during dissection and cannulation of the superior vena cava or IVC for the stage II cavopulmonary anastomosis or TCPC completion. One can speculate that surgical strategies that minimize operative dissection during these 2 latter stages of single ventricle palliation, such as deep hypothermic circulatory arrest, may be beneficial in reducing the incidence of iatrogenic phrenic nerve injury. It is more important to prevent diaphragmatic paralysis than to treat it.³⁰

Conclusions

In both biventricular and Fontan patients, diaphragm plication does not completely restore normal subdiaphragmatic venous fluid dynamics. In Fontan patients with a plicated diaphragm, inspiration-derived hepatic venous flow is suppressed and portal venous flow loses its normal expiratory augmentation. These flow dynamics share similarities with those observed in patients with failing Fontan circulation. This suboptimal splanchnic circulation may contribute to early problems of prolonged pleural effusion and ascites and potentially promote late Fontan failure. Phrenic nerve injury should consequently be avoided at all costs before or at the time of the Fontan operation.

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References

1. Brecher GA. Venous return. New York: Grune & Stratton; 1956.
2. Guyton AC. Venous return. In: Hamilton WF, editor. Handbook of physiology. Section 2: Circulation. Washington (DC): American Physiologic Society; 1963. p 1099-133.
3. Moreno AH, Burchell AR. Respiratory regulation of splanchnic and systemic venous return in normal subjects and in patients with hepatic cirrhosis. *Surg Gynecol Obstet.* 1982;154:257-67.
4. de Leval MR. The Fontan circulation: a challenge to William Harvey? *Nat Clin Pract Cardiovasc Med.* 2005;2:202-8.
5. Hsia TY, Khambadkone S, Deanfield JE, Taylor JF, Migliavacca F, de Leval MR. Subdiaphragmatic venous hemodynamics in the Fontan circulation. *J Thorac Cardiovasc Surg.* 2001;121:436-47.
6. Hsia TY, Khambadkone S, Redington AN, de Leval MR. Effect of fenestration on the sub-diaphragmatic venous hemodynamics in the total-cavopulmonary connection. *Eur J Cardiothorac Surg.* 2001;19:785-92.
7. Hsia TY, Khambadkone S, Redington AN, Migliavacca F, Deanfield JE, de Leval MR. Effects of respiration and gravity on infradiaphragmatic venous flow in normal and Fontan patients. *Circulation.* 2000;102(19 Suppl 3):III148-III153.
8. Amin Z, McElhinney DB, Strawn JK, Kugler JD, Duncan KF, Reddy VM, et al. Hemidiaphragmatic paralysis increases postoperative mor-

- bidity after a modified Fontan operation. *J Thorac Cardiovasc Surg.* 2001;122:856-62.
9. Ovroutski S, Alexi-Meskishvili V, Stiller B, Ewert P, Abdul-Khalik H, Lemmer J, et al. Paralysis of the phrenic nerve as a risk factor for suboptimal Fontan hemodynamics. *Eur J Cardiothorac Surg.* 2005; 27:561-5.
 10. Akay TH, Ozkan S, Gultekin B, Uguz E, Varan B, Sezgin A, et al. Diaphragmatic paralysis after cardiac surgery in children: incidence, prognosis and surgical management. *Pediatr Surg Int.* 2006;22:341-6.
 11. de Leeuw M, Williams JM, Freedom RM, Williams WG, Shemie SD, McCrindle BW. Impact of diaphragmatic paralysis after cardiothoracic surgery in children. *J Thorac Cardiovasc Surg.* 1999;118:510-7.
 12. Shoemaker R, Palmer G, Brown JW, King H. Aggressive treatment of acquired phrenic nerve paralysis in infants and small children. *Ann Thorac Surg.* 1981;32:250-9.
 13. Abu-Yousef MM. Normal and respiratory variations of the hepatic and portal venous duplex Doppler waveforms with simultaneous electrocardiographic correlation. *J Ultrasound Med.* 1991;11:263-8.
 14. Gibson GJ. Diaphragmatic paresis: pathophysiology, clinical features, and investigation. *Thorax.* 1989;44:960-70.
 15. Marcos JJ, Grover FL, Trinkler JK. Paralyzed diaphragm—effect of plication on respiratory mechanics. *J Surg Res.* 1974;16:523-6.
 16. Roussos C, Macklem PT. The respiratory muscles. *N Engl J Med.* 1982;307:786-97.
 17. Takeda S, Nakahara K, Fujii Y, Matsumura A, Minami M, Matsuda H. Effects of diaphragmatic plication on respiratory mechanics in dogs with unilateral and bilateral phrenic nerve paralyses. *Chest.* 1995;107: 798-804.
 18. Lemmer J, Stiller B, Heise G, Hubler M, Alexi-Meskishvili V, Weng Y, et al. Postoperative phrenic nerve palsy: early clinical implications and management. *Intensive Care Med.* 2006;32:1227-33.
 19. Joho-Arreola AL, Bauersfeld U, Stauffer UG, Baenziger O, Bernet V. Incidence and treatment of diaphragmatic paralysis after cardiac surgery in children. *Eur J Cardiothorac Surg.* 2005;27:53-7.
 20. Wheatley AM, Zhang X. Intrahepatic modulation of portal pressure and its role in portal hypertension. *Digestion.* 1998;59:424-8.
 21. Bradley SE. The hepatic circulation. In: Dow P, editor. *Handbook of physiology.* Washington (DC): American Physiological Society; 1963. p 1387-438.
 22. Greenway CV, Lault WW. Distensibility of hepatic venous resistance sites and consequences on portal pressure. *Am J Physiol.* 1988;254: H452-8.
 23. Redington AN, Penny D, Shinebourne EA. Pulmonary blood flow after total cavopulmonary shunt. *Br Heart J.* 1991;65:213-7.
 24. Donald D. Splanchnic circulation. In: Geiger SR, editor. *Handbook of physiology* Section 2: The cardiovascular system. Bethesda: American Physiologic Society; 1983. p 219-40.
 25. Brauer RW, Holloway RJ, Leong GF. Changes in liver function and structure due to experimental passive congestion under controlled hepatic vein pressures. *Am J Physiol.* 1959;197:681-92.
 26. Dunbar BS, Elk JR, Drake RE, Laine GA. Intestinal lymphatic flow during portal venous hypertension. *Am J Physiol.* 1989;257(1 Pt 1):G94-8.
 27. Esposito RA, Spencer FC. The effect of pericardial insulation on hypothermic phrenic nerve injury during open-heart surgery. *Ann Thorac Surg.* 1987;43:303-8.
 28. Helps BA, Ross-Russell RI, Dicks-Mireaux C, Elliott MJ. Phrenic nerve damage via a right thoracotomy in older children with secundum ASD. *Ann Thorac Surg.* 1993;56:328-30.
 29. Iverson LI, Mittal A, Dugan DJ, Samson PC. Injuries to the phrenic nerve resulting in diaphragmatic paralysis with special reference to stretch trauma. *Am J Surg.* 1976;132:263-9.
 30. Ozkan S, Akay T. Diaphragm paralysis in children after cardiac surgery. *J Cardiothorac Vasc Anesth.* 2007;21:164-5.

Discussion

Dr Brian L. Reemtsen (Los Angeles, Calif). I'd first like to congratulate the authors on an excellent presentation on a difficult subject. I have 3 questions in regard to your presentation. First, at our institution we have retrospectively reviewed all the patients that have undergone diaphragm plication after cardiac surgery, and

we have observed that all patients have some return of function at 1 year. Did you notice any return of function in these affected diaphragms? At what time intervals, if any, did you look at the diaphragms? Do you think that this improved function could lead to better splanchnic hemodynamics?

Dr Hsia. As far as your question about interval diaphragmatic interrogation is concerned, a recent article from The Netherlands reports 4 (29%) of 14 patients who had previous diaphragm plication have return of appropriate diaphragmatic movement during follow-up.¹ For this study, we enrolled patients with previous diaphragm plication, but without return of normal diaphragm function. Those with return of function noted from ultrasound interrogation were excluded from this study. For the 19 biventricular and Fontan patients studied with previous diaphragm plication, their affected diaphragm remained either immobile or fixated in place with no paradoxical motion under ultrasonographic interrogation.

Dr Reemtsen. My second question relates to the first one. In your manuscript you did not describe what method you used for plication. Could you briefly go through that and tell us whether you think that has any impact on possible return of function or splanchnic blood flow?

Dr Hsia. All diaphragm plications used a linear imbrication technique. This is also referred to as the accordion or central pleating method as described by Shoemaker and associates.² Therefore, I cannot speculate whether different techniques of diaphragmatic plication can lead to differential return of diaphragmatic function or variably affect splanchnic venous flow dynamics.

Dr Reemtsen. Finally, you related that the patients with diaphragm paralysis have impaired splanchnic hemodynamics stemming from altered respiratory mechanics. You made the corollary that this may, in fact, lead to poor Fontan hemodynamics. My question is, did these 9 patients have poor Fontans with high pressures and increased incidence of ascites and protein-losing enteropathy?

Dr Hsia. This is a very good question. We believe the basis of this study's significance is that our data shed light on a previously unknown consequence of phrenic nerve injury and diaphragm paralysis: that despite surgical plication, the flow dynamics is suboptimal. Because these suboptimal characteristics are similar to those seen in patients with failing Fontan circulation, those with a plicated diaphragm may be predisposed for earlier failure and thus benefit from a higher level of surveillance and clinical follow-up.

When this physiologic study was performed 6 years ago, none of the 9 Fontan patients had documented protein-losing enteropathy or elevated pressures. However, 1 was in NYHA class II and 3 were in class III. One patient in class III, or failing Fontan state, has since died. Unfortunately, we do not have information whether this patient had protein-losing enteropathy or other gastrointestinal problems. All 19 of the patients who were in NYHA class I after the Fontan operation, with normal diaphragms, remain in class I since conclusion of the study.

Discussion References

1. van Onna IE, Metz R, Jekel L, Woolley SR, van de Wal HJ. Post cardiac surgery phrenic nerve palsy: value of plication and potential for recovery. *Eur J Cardiothorac Surg.* 1998;14:179-84.
2. Shoemaker R, Palmer G, Brown JW, King H. Aggressive treatment of acquired phrenic nerve paralysis in infants and small children. *Ann Thorac Surg.* 1981;32:250-9.