Diaphragm Paralysis After Cardiac Surgery: A Frequent Cause of Post-Operative Respiratory Failure

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Keywords: diaphragm paralysis, cardiac surgery, coronary bypass grafting, pneumonia, mechanical ventilation

Posted Date: October 29th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-97833/v1

Abstract

Background

Diaphragmatic dysfunction (DD) is found in 1.2-60% of patients after cardiac surgery. The aim of this study was to reinvestigate the incidence, risk factors and outcomes of DD with actual cardiac surgery procedures.

Methods

This is an observational study based on a prospectively collected database in one cardiac surgery centre. The DD group included patients with clinically perceptible diaphragmatic paralysis, which was confirmed by chest ultrasound (amplitude of the diaphragm movement in time-motion mode [TM] at rest, after a sniff test). The primary endpoint was the incidence of DD.

Results

A total of 3577 patients were included between January 2016 and September 2019. We found 272 cases of DD (7.6%). Individuals with DD had more arterial hypertension (64.3% vs. 52.6%; p<0.0001), higher body mass index (BMI) (28[25–30] kg/m2 vs. 26[24-29] kg/m2; p<0.0002) and higher incidence of coronary bypass grafting (58.8% vs. 46.6%; p=0.0001). DD was associated with more postoperative pneumonia (23.9% vs. 8.7%; p<0.0001), reintubation (8.8% vs. 2.9%; p<0.0001), tracheotomy (3.3% vs. 0.3%; p<0.0001), non-invasive ventilation (45.6% vs. 5.4%; p<0.0001), duration of mechanical ventilation (5[4-11] h vs. 4[3-6] h; p<0.0001), and ICU and hospital stays (14[11-17] days vs. 13[11–16] days; p<0.0001). In multivariate analysis, DD was associated with coronary artery bypass grafting (OR=1.9[1.5-2.6]; p=0.0001), arterial hypertension (OR=1.4[1.1- 1.9]; p=0.008), and BMI (OR per point =1.04[1.01-1.07] kg/m2; p=0.003).

Conclusion

The incidence of symptomatic DD after cardiac surgery was 7.6%, leading to respiratory complications and increased ICU stay. Coronary bypass grafting was the principal factor associated with DD.

Background

Cardiac surgery has nearly a 6% rate of postoperative respiratory complications, which aggravate the patient prognosis [1–4]. Among these complications, diaphragmatic dysfunction (DD) has an unknown incidence, ranging from 1.2–60% [5–10]. DD impairs ventilatory mechanics, promotes pneumonia and sternal disjunction [11–13]. Past studies have identified several risk factors for postoperative DD, including age, diabetes, mammary artery harvesting, peri-operative cold solutions and extracorporeal circulation time [7, 14, 15]. However, actually, most cardiac interventions no longer use cold cardioplegia, [16] and coronary grafts are most often made using one or two mammary arteries [17, 18].

DD is suspected when post-operative acute respiratory dysfunction occurs with paradoxical ventilation and ascent of the diaphragmatic dome on the chest X-ray. The diagnosis can be confirmed by chest ultrasound, which finds a decrease in the amplitude of the movement of the diaphragm in time-motion mode (TM) [19–21].

DD can be transient after cardiac surgery and can be related to mechanical factors, such as pain, pleural effusion, presence of pleural and mediastinal tubes, decubitus position, and sternotomy, with recovery after a few days [22, 23]. It may be more prolonged in connection with partial or complete damage to the phrenic nerve and/or diaphragmatic devascularization [9, 24], with more prolonged or definitive effects [25].

The aim of our study was to investigate the actual incidence, risk factors and outcomes of patients who present with DD after cardiac surgery.

Material & Methods

This observational study was based on the analysis of a prospectively collected database. According to French national regulation, systematic written informed consent was requested for all patients on admission for the secured storage of clinical and para-clinical data obtained during hospitalization and for potential anonymous use in clinical research studies. All adult patients who underwent a cardiac surgery between January 2016 and September 2019 in one teaching hospital were included (Clinique Ambroise Paré, Neuilly-Sur-Seine, France). Operative indications for surgery agreed with the current European guidelines during the study.

Two groups were defined. The DD group included all patients with clinically perceptible post-operative diaphragmatic paralysis. The diagnosis of DD was suspected clinically and/or radiologically and confirmed by chest ultrasound. The diagnosis of DD was considered confirmed when a decrease in the TM amplitude of the movement of the diaphragm was found below the lower limit of normal for at least one of the following measurements: 1) at rest, < 9 mm for women and < 10 mm for men; 2) after a sniff test, < 16 mm for women and < 18 mm for men; and 3) after a deep inspiration, < 37 mm for women and < 47 mm for men [21]. The control group included all other patients.

The data collected included demographic and medical data; type of cardiac disease; EuroSCORE II; ECG findings; type of surgery; operating data, including duration of cardiopulmonary bypass (CPB) and aortic cross-clamping (ACC); pre- and post-operative echocardiography; and main complications after surgery, including use of inotropes, sepsis, pneumonia, ischaemia, stroke, reoperation, mediastinitis, length of stay and hospital mortality.

When DD was confirmed, patients were treated according to our local protocol, including half-sitting position, reinforced muscular and respiratory kinesitherapy, intermittent non-invasive ventilation, nocturnal continuous positive airway pressure therapy, and bowel prokinetic drugs, if necessary, using trimebutine 100 mg/24 h + erythromycin 375 mg/24 h + macrogol 26 g/ 24 h. If no transit was obtained after 48 h, neostigmine 1.5 mg/24 h subcutaneously was added.

The primary endpoint was the incidence of DD. Secondary outcomes were as follows: 1) the search of DD predictive factors among the collected data and 2) the main complication associated with DD as compared to the control group.

Statistical analysis

Shapiro-Wilk tests were used to test the normality of distribution of the studied variables. Continuous variables were expressed as mean ± standard deviation (SD) when distributed normally or median [interquartile range] when not. Categorical variables were expressed as a number (percentage). Categorical variables in two groups were compared using Chi-squared and Pearson's test. Comparison of variables normally distributed used Student's t test. Other continuous variables were compared by the Mann-Whitney U nonparametric test.

A multivariate analysis was conducted by a logistic regression, including comparisons with $p \leq 0.1$ in univariate analyses. A constant was added. All predictors were considered clinically meaningful, and none was rejected. The significance threshold adopted was $p < 0.05$. The software used was SPSS 25.0®, IBM®, Armonk United States.

Results

During the studied period, 3577 patients underwent cardiac surgery. Among them, 272 had DD. Baseline pre-operative characteristics of the whole cohort are presented in Table 1. Patients in the DD group had more arterial hypertension and higher body mass index (BMI) compared to the control group; other baseline characteristics were similar.

Table 1

Preoperative patient characteristics. DD: diaphragmatic dysfunction, BMI: body mass index, COPD: chronic obstructive pulmonary disease, EuroSCORE: European System for Cardiac Operative Risk Evaluation, LVEF: left ventricular ejection fraction, NYHA: New York Heart Association, PAPs: systolic pulmonary arterial pressure.

	DD (n = 272)	**No DD (n = 3305)**	**p**
Age (years), median	71 [62–78]	70 [62–77]	0.12
Male gender, n (%)	197 (72.4)	2465 (74.6)	0.43
BMI (kg/m^2)	28 [25–30]	26 [24–29]	< 0.0001
Arterial hypertension	175 (64.3)	1737 (52.6)	0.0002
Diabetes mellitus	83 (30.5)	869 (26.3)	0.13
Chronic renal failure requiring dialysis	3 (1.1)	42 (1.3)	0.81
Smoker status	79 (29.0)	1012 (30.6)	0.59
Prior atrial fibrillation	27 (9.9)	295 (8.9)	0.58
COPD	16 (5.9)	252 (7.6)	0.29
Pre-operative LVEF > 50%,	227 (83.5)	2819 (85.3)	0.41
Pre-operative LVEF 31–50%	42 (15.4)	417 (12.6)	0.18
Pre-operative LVEF ≤ 30%	3 (1.1)	69 (2.1)	0.27
Pre-operative PAPs > 35 mmHg	64 (23.5)	775 (23.5)	0.98
Pre-operative PAPs > 55 mmHg	13 (4.8)	167 (5.1)	0.84
EuroSCORE II	1.7 [1.94–3.14]	1.73 [0.97–3.24]	0.63
Prior cardiac surgery	23 (8.5)	284 (8.6)	0.94
Emergent or urgent surgery	22 (8.1)	287 (8.7)	0.74

Intra-operative patient characteristics are presented in Table 2. There was more isolated coronary bypass grafting in the DD group (58.8% vs. 46.6%; p = 0.0001) and less combined valve surgery. The number of coronary bypass grafting anastomosis was higher in the DD group (2 ± 1.4 vs. 1.4 ± 1.5; p < 0.0001). Cardiopulmonary bypass (CPB) and ACC time were similar in the two groups.

Table 2
Intra-operative patient characteristics. DD: diaphragmatic dysfunction, ACC: aortic cross-clamping, CPB: cardiopulmonary bypass, combined coronary surgery: coronary bypass plus valve or aortic surgery.

	DD (n = 272)	No DD (n = 3305)	p
Full sternotomy, n (%)	266 (97.8)	3219 (97.4)	0.69
ACC (min), median	58 [48–71]	59 [47–72]	0.81
CPB (min)	72.5 [60–96]	74 [60–92]	0.91
Coronary bypass grafting alone	160 (58.8)	1541 (46.6)	0.0001
Left mammary artery	159 (99.4)	1530 (99.3)	0.90
Right mammary artery	156 (97.5)	1478 (95.9)	0.33
Both mammary arteries	155 (96.9)	1469 (95.3)	0.37
Combined coronary-valve surgery	42 (15.4)	382 (11.6)	0.06
Left mammary artery	41 (97.6)	337 (88.2)	0.06
Right mammary artery	27 (64.3)	251 (65.7)	0.85
Both mammary arteries	27 (64.3)	208 (54.5)	0.22
Number of coronary bypass grafting anastomoses	2 ± 1.4	1.4 ± 1.5	0.0001
Valve surgery	68 (25)	1321 (40)	0.0001
Aortic surgery alone	7 (2.6)	63 (1.9)	0.45
Tricuspid surgery alone	1 (0.4)	33 (1.0)	0.29
Mitral valve surgery alone	22 (8.1)	333 (10.1)	0.29
Aortic valve surgery alone	34 (12.5)	626 (18.9)	0.009
Combined valve surgery	4 (1.5)	266 (8.0)	< 0.0001
Other	2 (0.7)	61 (1.8)	0.18

Post-operative outcomes are presented in Table 3. Patients in the DD group had significantly worse respiratory outcomes, including more pneumonia (23.9% vs. 8.7%; p < 0.0001), reintubation, tracheotomy, and non-invasive ventilation (45.6% vs. 5.4%, p < 0.0001), compared with the control group. They also had longer duration of mechanical ventilation and ICU and hospital stays. Postoperative creatine kinase peaks were significantly higher in the DD group compared with the control group (783[475–1133] UI/l vs. 553[389–890] UI/l; p < 0.0001), but the troponin peak was not different (2.9[1.4–6.5] vs. 2.6 [1.4–5.7] ng/ml; p = 0.34). Mortality was significantly lower in the DD group compared with the control group (0.7% vs. 2.9%; p < 0.03)

Table 3

Post-operative characteristics and outcomes. DD: diaphragmatic dysfunction, ICU: intensive care unit

Outcomes	DD (n = 272)	No DD (n = 3305)	p
Pneumonia	65 (23.9)	313 (8.7)	< 0.0001
Non-invasive ventilation	124 (45.6)	177 (5.4)	< 0.0001
Duration mechanical ventilation (hours)	5 [4–11]	4 [3–6]	< 0.0001
Tracheotomy	9 (3.3)	10 (0.3)	< 0.0001
Length of stay in hospital (days)	14 [11–17]	13 [11–16]	< 0.0001
Length of stay in ICU (days)	4 [4–5]	4 [4–5]	0.0006
Hospital mortality	2 (0.7)	97 (2.9)	0.03
Patent foramen ovale	6 (2.2)	28 (0.9)	0.03
New-onset atrial fibrillation	74 (27.2)	888 (26.9)	0.90
Reintubation	24 (8.8)	95 (2.9)	< 0.0001
Use of catecholamine	40 (14.7)	462 (14.0)	0.74
Cerebral ischaemic events	4 (1.5)	55 (1.7)	0.81
Deep sternal wound infection	6 (2.2)	46 (1.4)	0.28

Predictors of DD in univariate analysis are shown in Table 4. In multivariate analysis (Table 5), the predictive factors of DD were coronary bypass grafting (OR = 1.9[1.5–2.6]; p = 0.0001), arterial hypertension (OR = 1.4[1.1–1.9]; p = 0.008), and BMI (OR per point = 1.04[1.01–1.07] kg/m^2; p = 0.003). Details of the side of DD and their relationship with mammary artery harvesting are presented in Fig. 1.

Table 4

Predictors of diaphragm dysfunction in univariate analysis. CI: confidence interval, BMI: body mass index, COPD: chronic obstructive pulmonary disease, EuroSCORE: European System for Cardiac Operative Risk Evaluation, ACC: aortic cross-clamping, CPB: cardiopulmonary bypass, LVEF: left ventricular ejection fraction, PAPs: systolic pulmonary arterial pressure.

	Odd Ratio	**95% CI**	**p**
Age	1.01	0.99–1.02	0.09
Male gender	1.12	0.85–1.47	0.43
Hypertension	1.6	1.25–2.10	0.0001
Diabetes	1.23	0.94–1.61	0.14
Smoker status	0.93	0.71–1.21	0.57
BMI	1.05	1.03–1.08	0.0001
COPD	0.65	0.35–1.2	0.17
EuroSCORE II	0.99	0.96–1.02	0.54
ACC time	1.0	0.99–1.01	0.93
CPB time	1.0	1.0-1.003	0.69
PAPs > 35 mmHg	1.004	0.75–1.34	0.98
PAPs > 55 mmHg	0.94	0.53–1.68	0.84
LEVF > 50%	0.87	0.62–1.22	0.41
LEVF 30–50%	1.27	0.90–1.79	0.18
LEVF < 30%	0.52	0.16–1.67	0.28
Peripheral arterial disease	1.40	1.0-1.96	0.05
Prior cardiac surgery	0.98	0.63–1.53	0.94
Urgent surgery	0.93	0.59–1.46	0.74
Coronary bypass grafting	2.07	1.57–2.75	0.0001
Valve surgery	0.61	0.48–0.79	0.001
Aortic surgery	0.94	0.55–1.61	0.83

Table 5
Multivariate analysis. CI: confidence interval, BMI: body mass index, COPD: chronic obstructive pulmonary disease.

Variable	Odd Ratio	[95% CI]	p
Coronary bypass grafting	1.9	[1.5–2.6]	0.0001
Hypertension	1.4	[1.1–1.9]	0.008
BMI (per point)	1.04	[1.01–1.07]	0.003
COPD	0.6	[0.3–1.1]	0.12
Age (per year)	1.01	[0.99–1.02]	0.22
Valve surgery	0.96	[0.7–1.4]	0.84
Peripheral arterial disease	1.2	[0.8–1.7]	0.37
Diabetes	0.89	[0.7–1.2]	0.44

Discussion

Despite recent advances in cardiac surgery procedures, we found a 7.6% postoperative incidence of DD. To our knowledge, this is the largest study of DD after cardiac surgery. Not surprisingly, we found that DD was associated with respiratory complications and prolonged ICU and hospital stays. Half of the patients with DD required non-invasive ventilation and one-quarter developed pneumonia. DD was also the cause of 20% of all reintubations and of 50% of all tracheotomies. However, the early diagnosis and systematic therapeutic protocol allowed a low in-hospital mortality rate (0.7%) that was not different from other patients.

Indeed, DD must be treated specifically. Although spontaneous recovery can be observed within 96 h after extubation [1, 3, 4], complications may have started during this time delay. Non-invasive ventilation may help to improve respiratory capacity after extubation. Some authors have suggested to keep the patient under mechanic ventilation until recuperation of diaphragm function, even if a tracheotomy needs to be used [1, 3, 4]. Our local protocol, applied to the patients in this study, gave priority to early extubation; bringing the patient on the armchair as soon as possible with intense respiratory physiotherapy to re-educate the diaphragm; and systematic use of non-invasive ventilation with positive pressure, including continuous positive airway pressure during sleep, to maintain residual functional capacity as close as possible to normal. Tracheostomy was restricted to patients with persistent DD with respiratory failure needing reintubation. Although our mortality was low, this was not an objective of our protocol and controlled studies are needed to evaluate this strategy.

Respiratory complications with or without pneumonia are frequent (2–6%) after cardiac surgery, leading to an increase of hospital stay and mortality [1, 3, 4]. DD is probably an underestimated cause of respiratory failure through other complications, such as atelectasis and pneumonia.

Our study confirmed the link between DD, hypertension, BMI, and coronary bypass grafting but not with diabetes, as previously observed. The role of diabetes in this pathology is still unclear [14, 24]. DD can be transiently due to many factors, including pain, hyperglycaemia, sepsis, neuromyopathy, electrolyte disorders (such as hypophosphoraemia), mechanical harm by tubes, and pleural or pericardial effusion. Prolonged DD is most often the consequence of a phrenic nerve injury but may be caused by multiple factors. The use of ice slush for myocardial protection during CPB was a well-known cause of phrenic nerve injury in the past, but it is no longer in use [8, 26]. It is uncertain whether phrenic nerve injury is primarily related to direct surgical injury or to ligation of its blood supply during internal mammary artery (IMA) dissection, especially when using electric cautery. Stretching of the phrenic nerves during chest opening may also be a possible mechanism and may explain why BMI, which supposes higher strength to open the chest, was associated with DD in our study and in others [10, 27]. The anatomic relationship between the phrenic nerve and the IMA is inconstant, and thus, caution must be taken when dissecting this artery. Furthermore, the blood supply to the phrenic nerve comes from the pericardiophrenic artery, which is a branch usually originating from the upper 1 to 3 cm of the IMA. In the 1990s, when the IMA was harvested, the reported incidence of DD was very high, ranging from 42–69% [8, 28, 29], but it decreased with the knowledge of this pathology, improvement in surgical techniques and increase in surgeon’s skills. Almost three-quarters (72.3%) of patients with DD were found after coronary bypass grafting, with quite a perfect parallelism between the side of the IMA harvesting and the side of the DD (100% for left DD and 94% for right DD). In the same way, the higher post-operative creatine kinase peak in the DD group, without differences in the troponin peak, may cause ischaemia of phrenic muscle after IMA harvesting. Nevertheless, the last quarter of our patients with DD (25.7%) were found after valvular surgery, confirming that DD does not have a unique mechanism.

Our study has several limitations. First, being a monocentric study, the results correspond to a specific experience. The retrospective nature of the analysis brings only a low risk of bias since the database was prospectively collected on a registry. However, this prevents the assertion of the causal link of the observed associations. The DD incidence we studied was the incidence of clinically perceptible DD. A systematic analysis of DD will probably find a higher incidence. Furthermore, we did not report the link between the side of DD paralysis and the side of internal jugular vein catheterization, systematically placed before surgery, which could be another risk factor for phrenic nerve injury. Last, we only studied intra-hospital events without a long-term follow-up. Data from long-term outcomes would be interesting, especially to analyse the potential recovery.

Conclusion

Symptomatic DD was found in 7.6% of patients after cardiac surgery. It leads to an increase of respiratory complications, such as pneumonia and prolonged ventilation and ICU stay. Coronary bypass grafting with IMA harvesting was the principal factor associated with DD, along with obesity and systemic hypertension in multivariate analysis. Early diagnosis and appropriate support can probably minimize its consequences.

Abbreviations

ACC: aortic cross-clamping

BMI: body mass index

CI: confidence interval

CPB: cardiopulmonary bypass

DD: diaphragmatic dysfunction

ICU: intensive care unit

IMA: internal mammary artery

OR: odds ratio

TM: time-motion mode

Declarations

- Ethical Approval and Consent to participate : According to French national regulation, systematic written informed consent was requested for all patients on admission for the secured storage of clinical and para-clinical data obtained during hospitalization and for potential anonymous use in clinical research studies.

- Consent for publication: Not applicable.

- Availability of supporting data: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

- Competing interests: The authors declare that they have no conflict of interest.

- Funding: The authors received no specific funding for this work

- Authors' contributions: D.L, P.E, and P.S contributed to the design and implementation of the research. P.M.L, R.M, A.S and A.B analyzed and interpreted data. DL, MPL, PS were major contributors in writing the manuscript. All authors read and approved the final manuscript.

- Acknowledgements: Thank you to Emma Taylor from Proof Reading Services for her proofreading of this paper.

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Figures

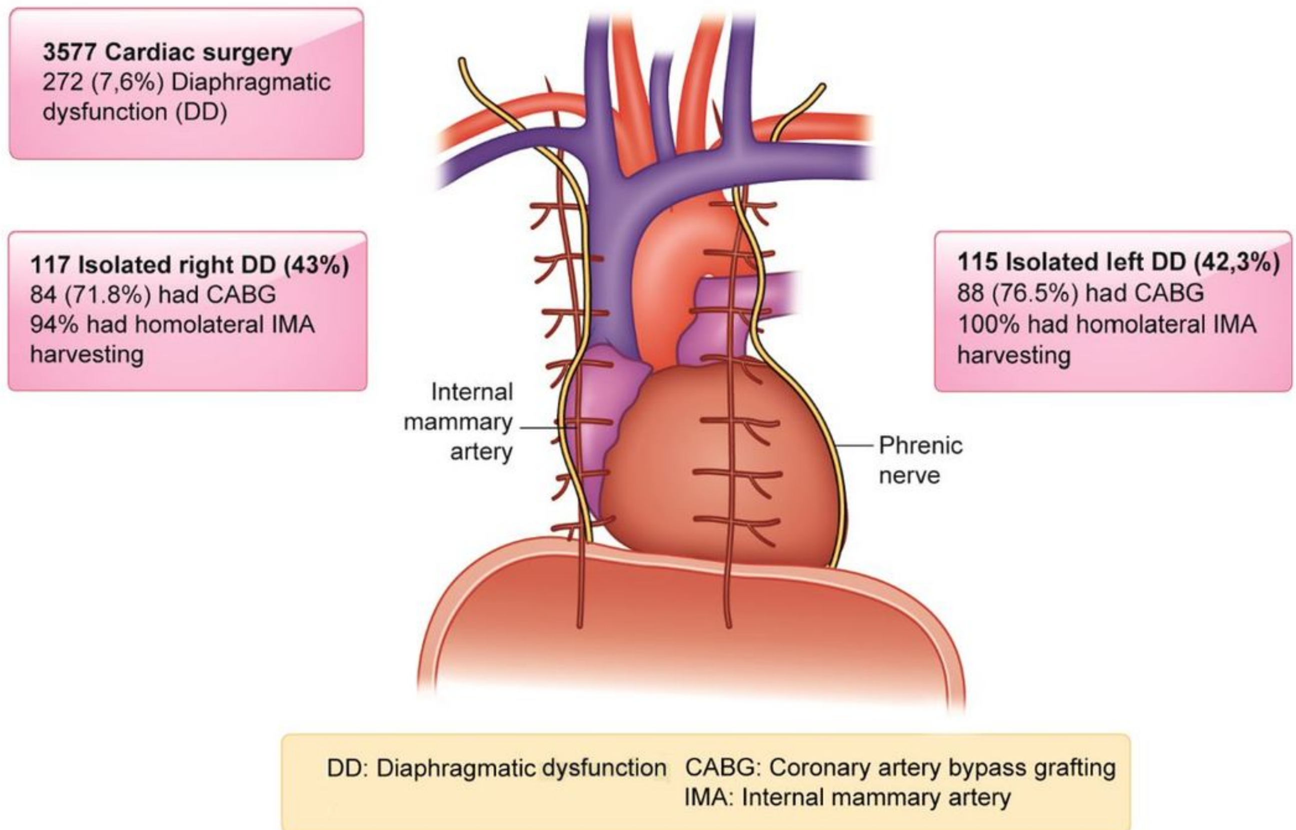

Figure 1

Diaphragmatic dysfunction and relationship with mammary arteries harvesting.