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Clinical Research

US National Trends in the Management and Outcomes of Constrictive Pericarditis: 2005-2014

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ABSTRACT

Background: Patient characteristics, trends in the management strategy, and outcomes of patients with constrictive pericarditis have not been characterized at the national scale.

Methods: Annual trends of patients admitted to hospitals in the United States with constrictive pericarditis were evaluated using the National Inpatient Sample dataset between 2005 and 2014. Poisson regression models adjusting for the US census population estimate were fitted to evaluate trends in the incidence of constrictive pericarditis, isolated pericardiectomy, and cardiopulmonary bypass (CPB) use. Descriptive analyses were performed to compare patient characteristics and in-hospital mortality rates between surgically and medically managed cohorts.

Results: During 2005-2014, 29,487 patients were admitted with constrictive pericarditis. Sixteen percent underwent isolated pericardiectomy. The prevalence of constrictive pericarditis remained stable between 2005 and 2014 at 9-10 cases per million, but proportion of patients undergoing isolated pericardiectomy decreased from 18% in 2005 to 15% in 2014 ($P = 0.001$ for trend). CPB use increased from 15% to 29% ($P < 0.001$). Compared with medically managed patients, the pericardiectomy cohort was younger (age 57 vs 61 years, $P < 0.001$), less likely to be female (25% vs 41%,

RÉSUMÉ

Contexte : Les caractéristiques des patients, les tendances en matière de stratégies de prise en charge et le devenir des patients atteints de péricardite constrictive n'ont pas été caractérisés à l'échelle nationale.

Méthodologie : Les tendances annuelles chez les patients atteints de péricardite constrictive hospitalisés aux États-Unis ont été évaluées à partir des ensembles de données du National Inpatient Sample couvrant la période allant de 2005 à 2014. Des modèles de régression de Poisson corrigés pour tenir compte de l'estimation de la population américaine effectuée lors du recensement ont été ajustés de façon à permettre l'évaluation tendancielle de la fréquence de la péricardite constrictive, de la péricardectomie isolée et du recours au pontage cardiopulmonaire (PCP). Des analyses descriptives ont été réalisées afin de comparer les caractéristiques des patients et les taux de mortalité intrahospitalière dans deux cohortes, l'une ayant été l'objet d'une prise en charge chirurgicale et l'autre, d'une prise en charge médicale.

Résultats : De 2005 à 2014, 29 487 patients atteints de péricardite constrictive ont été hospitalisés. Une péricardectomie isolée a été pratiquée chez 16 % d'entre eux. La prévalence de la péricardite constrictive est demeurée stable entre 2005 et 2014, s'établissant à 9 à 10 cas par million, mais la proportion de patients ayant subi une

Constrictive pericarditis is traditionally associated with poor outcomes, and the operative mortality for pericardiectomy remains high at 6% to 10%.[1-4] In the United States, the most common etiology is idiopathic, presumably due to prior viral pericarditis, followed by postcardiac surgery and postradiation therapy.[1] Tuberculous pericarditis resulting in constrictive pericarditis remains prevalent in other parts of the world.[5-7] Irrespective of the etiology, pericardiectomy is a class I recommendation by the 2015 European Society of Cardiology guideline in haemodynamically significant constrictive pericarditis.[8] Although a number of retrospective studies have described practice patterns often at single-centre scales,[1,5,6,9-17] the proportion of patients undergoing operative management and its temporal trend have not been evaluated at the national scale.

Owing to the technical complexity and limited reserve of the patients' cardiac functions, cardiopulmonary bypass (CPB) can be used as a backup measure, although the surgery itself is entirely extracardiac and does not require diastolic arrest with aortic cross-clamping and administration of

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$P < 0.001$), and harboured fewer comorbidities. In-hospital mortality was 7.3% for those undergoing pericardiectomy and 6.8% for a medically managed cohort ($P = 0.58$) and operative mortality was stable across years ($P = 0.99$ for trend).

Conclusions: The prevalence of constrictive pericarditis remained stable between 2005 and 2014 at 9-10 cases per million. Surgical management was infrequent, with younger and less comorbid patients being more likely to be managed operatively. Increasing use of CPB without a change in operative mortality highlights the persisting challenge of this complex disease.

péricardectomie isolée a diminué, passant de 18 % en 2005 à 15 % en 2014 ($p = 0{,}001$ pour la tendance). Le recours au PCP a augmenté, passant de 15 à 29 % ($p < 0{,}001$). Comparativement aux patients ayant été l'objet d'une prise en charge médicale, les patients formant la cohorte des péricardectomisés étaient plus jeunes (57 ans vs 61 ans, $p < 0{,}001$) et moins susceptibles d'être des femmes (25 % vs 41 %, $p < 0{,}001$) et ils présentaient moins de maladies concomitantes. Le taux de mortalité intrahospitalière a atteint 7,3 % chez les patients péricardectomisés et 6,8 % chez les patients de la cohorte ayant été l'objet d'une prise en charge médicale ($p = 0{,}58$), et la mortalité opératoire s'est avérée stable au fil des ans ($p = 0{,}99$ pour la tendance).

Conclusions : La prévalence de la péricardite constrictive est demeurée stable entre 2005 et 2014, s'établissant à 9 à 10 cas par million. La prise en charge chirurgicale a été peu fréquente; les patients plus jeunes et présentant moins de maladies concomitantes étaient plus susceptibles d'en être l'objet. Le recours croissant au PCP en l'absence de variation du taux de mortalité opératoire met en lumière le défi persistant que représente cette maladie complexe.

cardioplegia.[9] Decompression of the heart via CPB aids in dissecting the adhesive pericardium off the heart but potentially increases the risk of bleeding associated with full anticoagulation, as the operation creates a large, exposed surface area on the epicardium. The rate of CPB use is variable among centres, with the reported range from 1.7%[11] to 50.2%.[15] The trend in the use of CPB provides insights into the current operative strategy, but its use at the national level is unknown.

Using a nationally representative sample of hospital discharge records over the last decade, we aimed to characterize temporal trends in patient characteristics, management, and outcomes of patients with constrictive pericarditis.

Methods

Design and data definitions

A retrospective, annual, consecutive, cross-sectional study was performed to characterize trends in outcomes and management of patients admitted with constrictive pericarditis between 2005 and 2014, using the National (Nationwide) Inpatient Sample (NIS). The NIS is a large administrative database provided by the Agency for Healthcare Research and Quality that contains administrative and demographic data that represents approximately a 20% sample of all-payer inpatient hospitalizations in the United States, excluding federal hospitals.[18]

The Healthcare Cost and Utilization Project (HCUP) NIS dataset from 2005 to 2014 was used to characterize the prevalence, outcomes, and trends in operative and medical management of constrictive pericarditis. The NIS data only used International Classification of Diseases, Ninth Revision (ICD-9) codes during this period. The following discharge ICD-9-CM procedure and diagnosis codes were used to define constrictive pericarditis (423.2), pericardiectomy (37.31), and CPB use (39.61, 39.66). To better assess CPB use specifically for pericardiectomy, isolated pericardiectomy was defined by excluding cases with concomitant cardiac surgery: coronary artery bypass grafting (CABG), valve surgeries, and aortic surgeries (ICD codes defined in Supplemental Table S1).

Evaluated comorbidities were history of myocardial infarction (MI), diabetes, history of percutaneous coronary intervention, history of CABG, history of valve surgery, peripheral vascular disease (PVD), congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease (CKD), liver disease, morbid obesity, and immunosuppressed status. The list of variables and corresponding ICD-9-CM codes is shown in Supplemental Table S1. Age was categorized into 4 strata: ≤ 60 years, > 60 and ≤ 70 years, > 70 and ≤ 80 years, and > 80 years of age. Race was grouped into 4 categories: white, black, Hispanic, and others.

All investigators with access to the data have a signed Data-User Agreement with HCUP. This study was approved as an exempt from review by the Yale Human Investigations Committee.

Missing values

Age was missing in 2 observations and gender was missing in 1 observation. Because of the extremely low frequencies, these observations were excluded. Race was missing in 4842, and observations missing race data were categorized as a separate category of race to be included in the regression model. Comorbidities were coded by the presence or absence of corresponding diagnosis and procedure codes. Therefore, there were no missing values in this category.

Statistical analysis

In 2012, the sampling of NIS was redesigned to improve the accuracy of national estimates. To account for this change, HCUP has provided Trend Weight files (weight values to account for sampling used in the NIS) for years before 2012, which were used in our analysis after the HCUP's recommendation. This step was taken to improve the accuracy of national estimates across all years included in the analysis in response to the change in sampling design used

to generate the NIS dataset. SAS software Version 9.4 (SAS Institute Inc., Cary, NC) was used for all steps of the analysis. To provide the accurate estimate of standard errors account for the stratified cluster sampling design, SURVEY procedures were used with a hospital-level clustering for descriptive analyses as recommended by the HCUP.[18] Those with constrictive pericarditis were dichotomized into those undergoing pericardiectomy and those managed medically. Bivariate evaluations were performed using the Wilcoxon rank sum test, χ^2 test, and Fisher's exact test where appropriate. A logistic regression model was fitted for the likelihood of undergoing pericardiectomy among patients with constrictive pericarditis. The input variables for the model were age, race, sex, history of MI, history of valve surgery, history of CABG), PVD, congestive heart failure, chronic lung disease, CKD, liver disease, morbid obesity, and immunosuppressed status. Age, the only continuous variable in this study, was summarized by median and interquartile ranges. Multicollinearity was tested by examining variance inflation factor, with a cutoff of > 6 demonstrating significant multicollinearity, which none of the variables exceeded. In tables, categorical variables are summarized by percentages. Poisson regression models were fitted to evaluate trends in prevalence of constrictive pericarditis, incidence of pericardiectomy, and the proportion of CPB use. "Offset" function was used to adjust for the US census population for the prevalence of constrictive pericarditis and the incidence of pericardiectomy. Similarly, CPB use was adjusted for the total number of pericardiectomy cases. Calendar year as an ordinal variable was the only covariate included in the models. The trend of in-hospital mortality was tested using Poisson regression with calendar year as the covariate. Results are summarized with odds ratio and 95% confidence interval. Statistical significance is set at $P < 0.05$. Because of the relatively large sample size of the dataset, the contextual significance of the declining or increasing trend over time was evaluated not only by the P value (which would signify statistical significance), but also in conjunction with the relative or absolute change in the values.

Results

During 2005 to 2014, there were 29,487 hospital admissions with the diagnosis of constrictive pericarditis. Pericardiectomy, including isolated and concomitant pericardiectomy, was performed on 21.6% (6379 admissions), and isolated pericardiectomy was performed on 16.3% (4807 admissions) of all admissions with constrictive pericarditis. Patient characteristics are summarized in Table 1. Compared with medically managed patients, those undergoing pericardiectomy were younger (age 57 vs 61 years, $P < 0.001$), less likely to be female (25% vs 41%, $P < 0.001$), and generally harboured less comorbidities: history of MI (5.5% vs 18.4%, $P = 0.001$), diabetes (22.6% vs 26.2%, $P = 0.017$), prior CABG (3.2% vs 9.4%, $P < 0.001$), PVD (4.8% vs 6.7%, $P = 0.03$), and CKD (19.1% vs 25.1%, $P < 0.001$). In-hospital mortality was 7.3% for those undergoing pericardiectomy and 6.8% for medically managed cohort ($P = 0.58$).

Temporal trends in the management characteristics are summarized in Table 2 and Figure 1. The prevalence of constrictive pericarditis remained relatively stable between 2005 and 2014 at 9-10 cases per million with a minimal increase of 0.14 case per million per year; however, this slight increase was statistically significant ($P < 0.001$ for trend). The proportion of patients undergoing isolated pericardiectomy for constrictive pericarditis decreased over time from 18% in 2005 to 15% in 2014 at a rate of −0.3% per year ($P = 0.001$ for trend). CPB use increased over the decade from 15% to 29% ($P < 0.001$ for

Table 1. Patient characteristics and mortality

Variables	Pericardiectomy (n = 4807)	Percentage or IQR	Medical management (n = 24,680)	Percentage or SE	*P* value
Age (y, median, IQR)	57.6	49-67	61.1	51-74	**< 0.001**
Female	1224	25.5%	10,215	41.4%	**< 0.001**
Race					
White	3158	65.7%	15,701	63.6%	**< 0.001**
Black	272	5.7%	1569	6.4%	
Hispanic	201	4.2%	1569	6.4%	
Other	227	4.7%	1130	4.6%	
Missing	948	19.7%	3894	15.8%	
Comorbidity					
Myocardial infarction	262	5.5%	4544	18.4%	**0.001**
Diabetes	1088	22.6%	6472	26.2%	**0.017**
PCI	186	3.9%	1262	5.1%	0.099
Previous CABG	155	3.2%	2322	9.4%	**< 0.001**
Previous valve surgery	158	3.3%	1067	4.3%	0.12
PVD	233	4.8%	1656	6.7%	**0.031**
Heart failure	2444	50.8%	13,053	52.9%	0.25
COPD	793	16.5%	4399	17.8%	0.30
CKD (no dialysis)	916	19.1%	6185	25.1%	**< 0.001**
Dialysis-dependent CKD	68	1.4%	642	2.6%	**< 0.001**
Liver	778	16.2%	3262	13.2%	**0.014**
Morbid obesity	285	5.9%	1261	5.1%	0.29
Immunosuppressed	93	1.9%	353	1.4%	0.26
In-hospital mortality	352	7.3%	1681	6.8%	0.58

Bold *P* values indicate values < 0.05.

CABG, coronary artery bypass graft; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SE, standard error.

Table 2. Temporal trends in the operative management and CPB use for constrictive pericarditis

	Constrictive pericarditis*		All pericardiectomy*		Isolated pericardiectomy*		Isolated pericardiectomy with CPB*	
Year	Estimated N	Per million	Estimated N	Percentage of CP	Estimated N	Percentage of CP	Estimate	Percentage of isolated PC
2005	2666	9.0	668	25.1%	480	18.0%	74	15.4%
2006	2654	8.9	616	23.2%	441	16.6%	79	17.9%
2007	2651	8.8	547	20.6%	433	16.3%	116	26.9%
2008	2948	9.7	676	22.9%	490	16.6%	103	21.0%
2009	3223	10.5	792	24.6%	555	17.2%	152	27.5%
2010	2914	9.4	612	21.0%	519	17.8%	88	17.0%
2011	2834	9.1	544	19.2%	382	13.5%	81	21.2%
2012	3030	9.6	665	21.9%	505	16.7%	120	23.8%
2013	3205	10.1	620	19.3%	495	15.4%	160	32.3%
2014	3360	10.5	640	19.0%	505	15.0%	145	28.7%

CP, constrictive pericarditis; CPB, cardiopulmonary bypass; Estimated N, estimated sample size; PC, pericardiectomy; per million, prevalence per million persons of US census population.

*$P < 0.001$ for trend.

trend). There was no statistically significant change in in-hospital mortality after pericardiectomy for constrictive pericarditis over the study period ($P = 0.99$ for trend).

Discussion

Several salient findings of this study are the following: (1) pericardiectomy is performed only in one-fifth of all hospital admissions with constrictive pericarditis; (2) patients who were younger, male, and with fewer comorbidities were more likely to undergo the operation; and (3) the proportion of isolated pericardiectomy performed with CPB increased between 2005 and 2014 with a relative stability in the operative mortality over time.

Our finding of pericardiectomy being performed in a minority constrictive pericarditis despite being a class I recommendation by the European Society of Cardiology[8] generates several hypotheses and highlights areas in need of further investigations. Currently, the guideline states that "the mainstay of treatment of chronic permanent constriction is pericardiectomy," which leaves room for variable interpretation on what constitutes operative indications. It is possible that the medically managed patients did not warrant pericardiectomy based on the providers' assessment related to the likelihood of resolution or the severity of symptoms, but, currently, there exists no consensus on further operative indications. The decision likely varies across surgeons and centres. The surgery is undoubtedly of high risk, and it is also possible that some of the medically managed patients were perceived to harbour prohibitive risk to undergo the operation. Quantitative guidance on the predicted risk of adverse event after pericardiectomy is extremely limited. A study using the NIS dataset by Gopaldas et al[2] identified age, female sex, comorbidity index, and primary diagnosis as independent predictors of in-hospital mortality and complications for patients undergoing pericardiectomy. Although the study identified important risk factors for adverse events, further studies must evaluate granular haemodynamic parameters to provide a comprehensive understanding of patient characteristics that may be benefited or harmed by the operation. Accomplishing

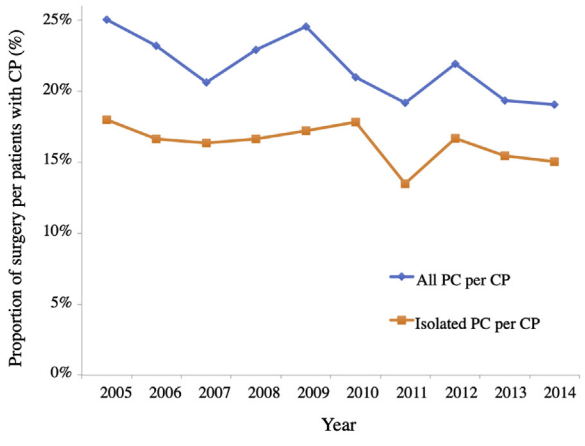

Figure 1. Trend in proportion of isolated and concomitant pericardiectomy for constrictive pericarditis between 2005 and 2014. The figure demonstrates a temporal decline in the proportion of patients with constrictive pericarditis undergoing isolated or concomitant pericardiectomy. CP, constrictive pericarditis; PC, pericardiectomy.

Table 3. Variables associated with nonoperative management of constrictive pericarditis

Variable	Odds ratio*	95% CI	*P* value
Age (per 1-y increase)	0.99	0.98-0.99	**< 0.001**
History of MI	0.63	0.44-0.89	**0.009**
Black race (ref. white)	0.52	0.37-0.71	**< 0.001**
Hispanic (ref. white)	0.58	0.41-0.83	**0.003**
Other race (ref. white)	0.98	0.68-1.40	0.89
Female	0.46	0.39-0.55	**< 0.001**
History of CABG	0.25	0.16-0.41	**< 0.001**
History of valve surgery	0.84	0.55-1.29	0.43
PVD	0.70	0.49-1.00	0.050
CHF	1.08	0.91-1.28	0.40
COPD	0.98	0.80-1.20	0.85
CKD (nondialysis)	0.80	0.66-0.97	**0.026**
CKD (dialysis)	0.55	0.28-1.06	0.074
Liver disease	1.22	0.99-1.50	0.062
Morbid obesity	0.96	0.69-1.35	0.83
Immunosuppressed	1.08	0.58-2.02	0.80

Bold *P* values indicate values < 0.05.

CABG, coronary artery bypass grafting; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease.

*Odds ratio > 1 indicates an increase in the odds of operative management. For example, the odds ratio of 0.99 per 1-y increase in age indicates lower odds of operative management with an increase in age.

this would require a large series containing both surgically and medically managed cohorts.

In this study, via multiple regression modelling, we characterized factors that may dictate the decision to undergo pericardiectomy. The model identified increased age, history of MI, non-white race, female sex, prior CABG, and CKD as factors associated with the increased likelihood of the patient not undergoing pericardiectomy (Table 3). This finding suggests that patient characteristics drive a selection against those who are perceived to be at higher risk. However, in the absence of robust risk model and guidelines based on quantified predicted risk of adverse events, such perception of risk likely varied across surgeons and centres. Another important element that may have impacted patient selection for pericardiectomy is the long-term survival forecasted at the time of patient selection. Long-term survival appears to be most consistently influenced by patient age and symptoms of heart failure at presentation,[10,15,16] although other risk factors, including diabetes and lung disease, have been described.[19] Whether such data have guided patient selection is unknown but is of important consideration in the future. Our study was limited to assess only the in-hospital mortality without longer-term follow-up. Therefore, in-hospital mortality rate between surgical and medical populations should not be interpreted as operative intervention yielding a higher mortality rate.

Although not investigated in this study, the subtype of constrictive pericarditis is an important consideration with regard to long-term survival. Such subtypes include transient constrictive pericarditis, effusive-constrictive pericarditis, and chronic constrictive pericarditis.[8] This was not captured within this analysis, as ICD-9 coding did not allow for this discrimination. The outcomes differ between the subgroups, and the providers' knowledge of this difference may have affected the perceived surgical candidacy. Likewise, etiology, which is also not captured in this analysis, is associated with outcomes after pericardiectomy,[15] and the etiology may have been part of guiding the patient selection.

Overall, through the study period, the incidence of constrictive pericarditis remained relatively stable, but the proportion of patients with constrictive pericarditis undergoing operative management decreased significantly. The utilization of CPB has increased from 15.4% in 2005 to 28.7% in 2014 with no significant change in operative mortality. Murashita et al.[15] described a similar increase in utilization rate over a longer time period at their institution in the United States, from 11.2% before 1990 to 62.7% in the modern era.[15] The increase in CPB utilization may be due to a decline in the risk of significant bleeding via improvement in haemostatic tools or miniaturization of CPB circuits that reduces inflammation and propensity for bleeding. It is also possible that increasing patient complexity, poorer haemodynamic reserve, and overall perceived risk of completing such cases off-pump may have resulted in this increase.

Because its conception in 1898, pericardiectomy has been recommended by the guideline as the definitive treatment of constrictive pericarditis.[8,20] Significant symptomatic improvement has been demonstrated after pericardiectomy,[19] but the current guideline remains vague in the operative indication. Our study suggests that pericardiectomy may be underutilized. Not accounting for clinical variables that may indicate disease severity, there appeared to be selection differentials against those with more comorbidity, female, and non-white race. Further investigation is needed to establish clear surgical indications to guide data-driven patient selection.

Limitations

Aside from the inherent limitations harboured in a retrospective analysis of claims-based data, the lack of indicator variable that allows for discrimination of diagnosis present on admission and those developed during hospitalization introduced room for misclassifying comorbidity as complications and vice versa. The set of comorbidity variables was selected specifically to minimize this misclassification. We also refrained from analysing complications for this reason. Clinical indicator variables, such as echocardiographic data and patient symptoms that may dictate decision to undergo operation, were not available in the administrative data. In addition, as the NIS captures only hospitalizations, the data do not allow for evaluation of the prevalence and nature of outpatient management, although the acuity of this pericarditis is likely to warrant inpatient management. Because longitudinal linkage of the data at patient level is not possible with the NIS data, it is likely rare but possible that patients with constrictive pericarditis who underwent pericardiectomy at previous hospitalizations could have been coded as having the diagnosis of constrictive pericarditis on the index hospitalization. Similarly, those medically managed initially could have been transferred to a hospital where they ultimately received surgical treatment, although the incidence of such transfer is unknown.

Conclusions

The prevalence of constrictive pericarditis remained relatively stable between 2005 and 2014 at 9-10 cases per million, but the proportion of patients undergoing pericardiectomy decreased over time. Only 16% underwent isolated pericardiectomy, with younger male with less comorbidity more likely to be managed operatively. The use of CPB increased over the decade without a change in operative mortality, highlighting the persisting challenge of this complex disease.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.05.015.