

Validity of a Hypertrophic Cardiomyopathy Diagnosis in Adult Patients in the Danish National Patient Register

Tino Severinsen^{1,2}, Helga Lillian Gudmundsdottir^{1,2}, Anna Axelsson Raja^{2,3}, Emil Loldrup Fosbøl^{2,3}, Henning Bundgaard^{2,3}, Jens Jakob Thune^{1,2}

¹Department of Cardiology, Copenhagen University Hospital - Bispebjerg and Frederiksberg, Copenhagen, Denmark; ²Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; ³Department of Cardiology, The Heart Center, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark

Correspondence: Jens Jakob Thune, Department of Cardiology, Copenhagen University Hospital - Bispebjerg and Frederiksberg, Nordre Fasanvej 57, Frederiksberg, 2000, Denmark, Tel +45 50470723, Email Jens.Jakob.thune@regionh.dk

Purpose: To assess the positive predictive value (PPV) of the diagnostic codes for hypertrophic cardiomyopathy (HCM) in the Danish National Patient Register (DNPR) and identify factors affecting the PPV.

Patients and Methods: We randomly sampled 200 patients registered in DNPR with the diagnostic codes DI421 (obstructive) or DI422 (non-obstructive) HCM, from Eastern Denmark, between December 1st, 2017, and September 16th, 2021. We assessed patients' medical records and classified whether the diagnosis of HCM was correct, incorrect, or uncertain according to the European Society of Cardiology (ESC) guidelines. Overall PPVs were estimated for all hospitals irrespective of specialty and for dedicated centers for inherited cardiac diseases.

Results: Of the 200 patients, seven were excluded; six were younger than 18 years when initially diagnosed and one adult patient had requested that their medical records be unavailable for research purposes. Of the 193 patients (median age 61 years, Interquartile range (IQR) 50–70, 40% female) with medical records available for assessment, 148 (77%) patients were registered correctly, 41 (21%) were incorrectly registered and for four (2%) patients there was insufficient data to determine if the diagnosis was correct. The overall PPV was 0.77 (95% confidence interval (CI) 0.70–0.82). The PPV for patients diagnosed in dedicated centers for inherited cardiac diseases was 0.91 (95% CI 0.84–0.95). For patients diagnosed in a dedicated center for inherited cardiac diseases with more than one clinical visit, the PPV increased to 0.99 (95% CI 0.93–1), however with the risk of a reduced sensitivity as these patients constituted only 52% of the correctly registered patients.

Conclusion: The overall PPV of the HCM diagnostic codes in the DNPR was 0.77 (95% CI 0.70–0.82). The validity of the diagnosis was higher at dedicated centers for inherited cardiac diseases. These findings may prove useful for future register-based research.

Keywords: Register, hypertrophic cardiomyopathy, Denmark, sample filters

Introduction

Hypertrophic cardiomyopathy (HCM) is characterized by left ventricular hypertrophy, impaired left ventricular relaxation, and hypercontractility.¹ The diagnosis is based on increased left ventricular wall thickness of at least 15 mm (13 mm in the case of confirmed HCM in a first-degree relative), which cannot be explained by loading conditions such as hypertension or aortic stenosis.^{2,3} The prevalence of HCM is estimated to be 1:500 individuals in the population.^{3–6} In approximately 30–60% of patients, a pathogenic or likely pathogenic variant can be identified in the genes encoding components of the cardiac sarcomere.² The clinical course of HCM is heterogeneous and can range from no symptoms to severe complications such as heart failure, ventricular tachycardia, atrial fibrillation, and sudden cardiac death.¹

Danish registries provide a valuable source of linkable, longitudinal data for the entire Danish population and may be used to assess the clinical trajectories of patients with HCM, but reliability of register-based research depends on the

validity of the registered data. However, the reliability of the individual diagnoses in the Danish National Patient Register (DNPR) varies, emphasizing the importance of validation before using a specific diagnosis for research.⁷ Validation studies with more than 100 patients for each diagnosis have documented a positive predictive values (PPV) of 0.76–0.84 for heart failure, 0.97–1 for myocardial infarction, 0.95 for atrial fibrillation and flutter, 0.82 for endocarditis, and 0.92 for pericarditis.^{8–11} However, the validation of the HCM diagnosis in Denmark has been limited to two significant studies with differing results. One of these studies, conducted in the Central Denmark Region (Catchment area 1.2 million inhabitants), included 20 patients from three hospitals. This study reported a PPV of 0.9 (95% confidence interval (CI) 0.7–0.97).¹¹ In contrast, a more recent single-center study from Odense University Hospital, which serves a similar catchment area of 1.2 million inhabitants (21% of the Danish population in 2021), reported a PPV of 0.68.¹² Two previous studies from Sweden have also demonstrated a wide range in the PPV of HCM diagnostic codes. In these studies, which included 129 and 184 patients respectively, the PPV was reported to range from 0.68 to 0.88.^{13,14} Given the heterogeneous disease presentation and overlap with other conditions associated with left ventricular hypertrophy, there is a risk of misregistration and misclassification of HCM in registries.

The purpose of this study was to validate the HCM diagnosis in the DNPR. Furthermore, this study aimed to identify factors that would increase or decrease the PPV, which could improve future register-based research's ability to sample true positive HCM patients.

Methods

Setting

The Danish healthcare system is tax-funded, providing free-of-charge care to both general practitioners and hospitals to all citizens. National and international guidelines recommend that first-degree relatives of patients with HCM are offered clinical and genetic assessment. The DNPR contains data on all patients discharged from Danish hospitals, encompassing both outpatient visits and admissions, in accordance with the International Statistical Classification of Diseases and Related Health Problems (ICD) codes. Registration in the DNPR is mandatory for both private and public hospitals, with the diagnostic codes being recorded by the physician responsible for the patient's treatment at the time of discharge/outpatient visit. Once logged in the DNPR, a diagnostic code cannot be modified or omitted from subsequent sampling.

Study Population and Data Collection

Patients eligible for inclusion in this study were adult patients (aged 18 years and older), registered with a diagnosis of obstructive or non-obstructive HCM (I42.1 and I42.2) in the Capital Region or Region Zealand between December 1st, 2017, and September 16th, 2021. The study population was based on a search from the DNPR; the search process and filters are described in Figure 1.

The electronic medical records of the sampled patients were reviewed systematically by one observer. This review included documentation of the patient's comorbidities and results of imaging studies. Additionally, results from genetic testing and cardiac magnetic resonance imaging (MRI) were recorded. After the initial review, the registered HCM diagnosis was classified as either correct, incorrect, or uncertain based on the collected data. A HCM registration was deemed correct if the left ventricular wall thickness was at least 15 mm (13 mm in the case of confirmed HCM in a first-degree relative) which could not be attributed to other causes of left ventricular hypertrophy. We did not discern between HCM diagnosis with or without obstruction as this may fluctuate over time and with treatment. Patients with specific storage- and metabolic disorders, which are included in the umbrella definition of HCM by the European Society of Cardiology (ESC), were not included in the final HCM population in the current study since these specific diagnoses have dedicated ICD codes, and validation of these diagnoses were outside the scope of the present study.^{2,3} Patients were registered as genotype positive if the patient record stated that a genetic test had shown a genetic variant considered likely pathogenic or pathogenic. We estimated the number of physicians involved in establishing or confirming the diagnosis based on health record descriptions and findings at the initial diagnostic workup and classified it as either a single physician or two or more physicians. The hospital that initially recorded the diagnostic code in the DNPR was registered as the responsible hospital for the diagnosis, irrespective of any subsequent referrals for confirmation. The time

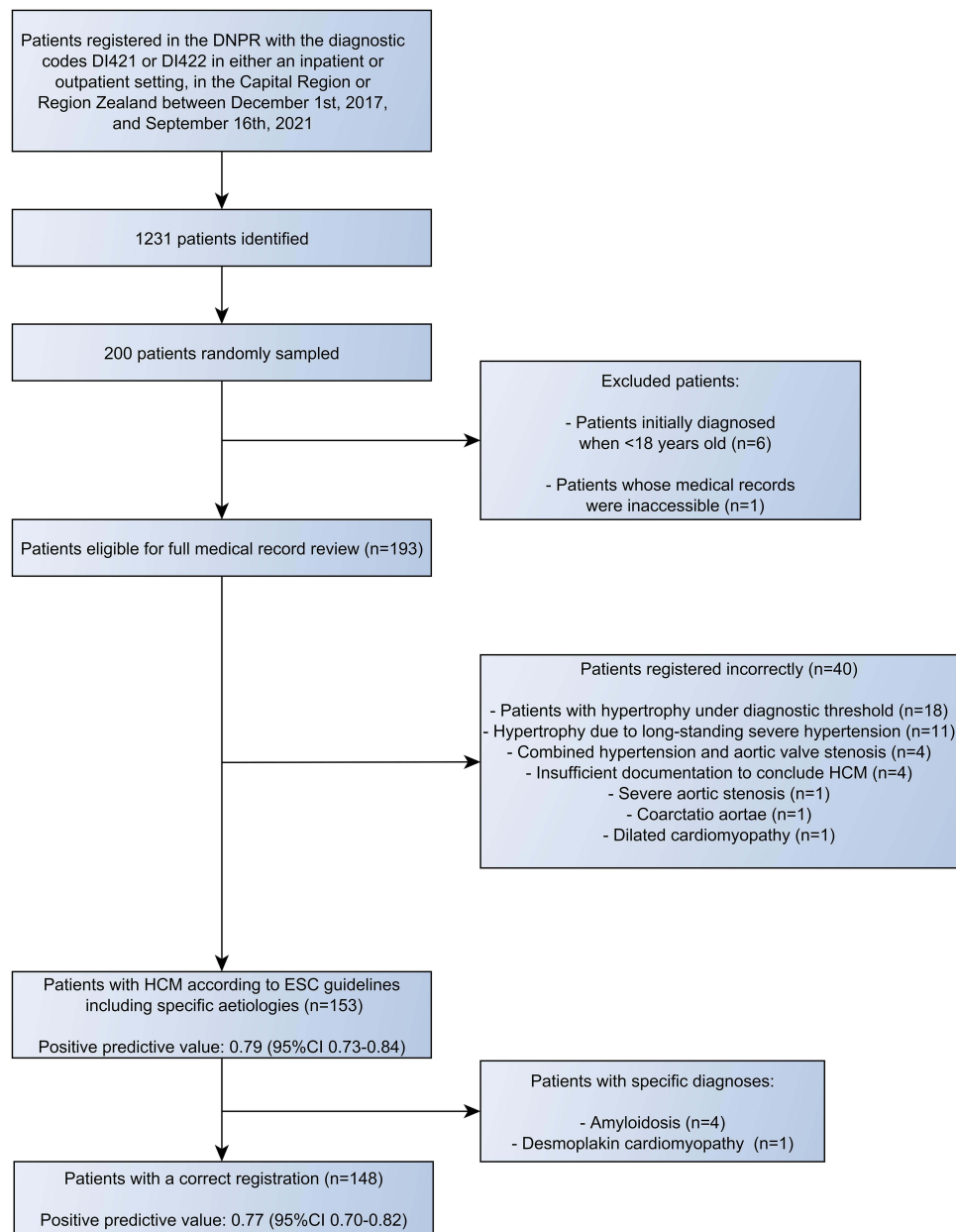


Figure 1 Flowchart of the inclusion process.

of diagnosis was determined by the first instance the diagnostic code was recorded. Data associated with the time of diagnosis were derived from this initial visit and any closely following clinical visits, during which baseline characteristics of the newly diagnosed patients were documented or verified. A center for inherited cardiac diseases was defined as a hospital department with an outpatient clinic, nurses or counsellors, and physicians dedicated to the management of inherited cardiovascular disease including family cascade screening. Six out of sixteen hospitals in Region Zealand and the Capital Region have a dedicated center for inherited cardiac diseases. A diagnosis was deemed uncertain if the patient was still undergoing diagnostic workup or if there was insufficient documentation to determine if the diagnosis was correct. The HCM registration was deemed incorrect if medical records revealed other causes of hypertrophy or if the patient did not fulfill the diagnostic criteria for left ventricular wall thickness. If the registration was considered incorrect, uncertain, or if the initial reviewer had any degree of doubt, the patient record and available imaging were reviewed by two cardiologists with extensive experience in diagnosing HCM to validate the registration. Initially, the cases were

reviewed separately to reduce bias, and in the event of disagreement between the two experts, the records were reviewed together to reach a consensus. For patients for whom the original records were unavailable, the diagnosis of HCM was instead confirmed using one or more subsequent echocardiographies and later journal entries from follow-up visits regarding their HCM diagnosis. In instances where data at the time of diagnosis was absent, the corresponding variable was excluded from the calculation of baseline characteristics.

Statistical Analysis

Categorical data for this study were described as frequencies and percentages. Continuous values were expressed as median values and interquartile range (IQR). To calculate p-values we used Pearson's chi-square test for categorical data and the Kruskal–Wallis test for numerical data. A p-value <0.05 was considered statistically significant. The validity of the diagnosis was reported as PPV. The CI of the PPV was calculated using the Wilson score method.¹⁵ With an assumed PPV of 0.85, a sample of 200 patients would provide a CI of approximately ± 0.05 . We conducted a multivariable logistic regression analysis of variables available in the DNPR to assess factors affecting the PPV of the HCM diagnosis. The variables included were age at the time of diagnosis, inpatient or outpatient status, whether the diagnosis was determined in a dedicated center for inherited cardiac diseases or a referral center, and number of clinical visits in the DNPR. An additional analysis was performed to determine the interactions between the abovementioned factors. All analyses and calculations were performed in R version 4.1.2.

Ethical Considerations

According to Danish law, register studies and patient record review studies do not require approval from the ethics committee. The data accessed as part of this study was treated in compliance with the relevant data protection and privacy regulations. This validation study was approved by the Center of Regional Development (Journal-number: R21002004).

Results

Baseline Characteristics

The 200 patients that were randomly sampled had a total of 1200 clinical visits relating to HCM, between December 1st, 2017, and September 16th, 2021, ranging from a single clinical visit (n=33) to 45 clinical visits (n=1). Seven patients were excluded, six patients were younger than 18 years and for one patient the medical records could not be accessed as this patient had requested his medical records be unavailable for research purposes. In total 193 patients (median age 61 years (IQR 50–70), 40% female) were available for a full medical record review. Baseline characteristics of the population are presented in Table 1. The inclusion process is visualized in Figure 1. After the initial review, 69 patients (36%) were reassessed by the two cardiologists separately. Among these, 20 cases had initial disagreements and were subsequently reviewed together to reach a consensus. From the medical records, we were able to see full echo/cardiac MRI reports or original images for 165 (85%) patients, genetic testing results for 193 (100%) patients, and family history for 193 (100%) patients.

Characteristics of Patients with a Correct Diagnosis of HCM

The registration of HCM was found to be correct in 148 (77%) patients, while the diagnosis was incorrectly registered as HCM in 41 (21%) patients and uncertain in four (2%). The four uncertain patients were counted as incorrectly registered, as we did not find that the patients had been examined well enough to conclude HCM before registering a diagnosis, making the total of incorrect diagnoses 45 patients. Therefore, the overall PPV in the DNPR of the diagnostic codes was 0.77 (95% CI 0.70–0.82) in our sample of 193 patients.

In patients in whom the imaging reports were available (n=172), septal hypertrophy was registered in 98 patients (57%), apical hypertrophy in 19 patients (11%), concentric hypertrophy in 44 patients (25%) while eight patients (5%) did not have hypertrophy. Three patients (2%) had at the time of diagnosis both septal and apical hypertrophy and one patient (1%) had both apical and concentric hypertrophy.

Table I Baseline Characteristics of the Patients Eligible for Full Medical Record Review

	All Patients	Correctly Classified	Incorrectly Classified	P-value
All patients	193	148	45	
Age at time of diagnosis, years	61 (50–70)	59 (47–68)	68 (56–80)	0.009
Female	77 (40%)	58 (39%)	19 (42%)	0.8
Comorbidities at the time of diagnosis				
Hypertension	81 (50%)	51 (43%)	30 (70%)	0.004
Valvular disorders	2 (1%)	1 (1%)	1 (2%)	1
Left ventricle ejection fraction <50%	17 (11%)	10 (8%)	7 (16%)	0.2
Atrial fibrillation	27 (17%)	20 (17%)	7 (16%)	1
Chronic obstructive pulmonary disorder	7 (4%)	4 (3%)	3 (7%)	0.6
Dyslipidemia	58 (36%)	41 (34%)	18 (42%)	0.5
Prior stroke	10 (6%)	5 (4%)	5 (12%)	0.2
Coronary artery disease	19 (12%)	14 (12%)	5 (12%)	1
Diabetes type 2	19 (12%)	14 (12%)	6 (14%)	0.9
Number of comorbidities	1 (0; 2)	1 (0; 2)	2 (1; 3)	0.001
Cardiac imaging				
Cardiac MRI performed	41 (21%)	40 (27%)	1 (2%)	0.0002
Original echocardiography report available from time of diagnosis	167 (87%)	125 (84%)	42 (93%)	0.2
Cardiac MRI performed and original echocardiography report available from the time of diagnosis	38 (20%)	37 (25%)	1 (2%)	1
Left ventricle maximum wall thickness at the time of diagnosis, mm	16 (15–18)	17 (16–19)	15 (12–16)	<0.0001
Left ventricle outflow tract obstruction at the time of diagnosis, >30 mmHg	48 (30%)	38 (26%)	10 (24%)	1
Family screening and genetics				
Pathogenic or likely pathogenic variant	44 (38%)	43 (29%)	1 (2%)	0.0005

Notes: Data are presented as n (%) or median (IQR); due to missing data, the denominator for percentages varies.

Abbreviations: IQR, Interquartile range; MRI, Magnetic resonance imaging.

Reasons for Misclassification

The correct diagnosis and cause of hypertrophy of the 45 patients incorrectly registered as HCM is presented in [Figure 1](#). 18 of the 45 individuals (40%) did not meet the established maximal left ventricular wall thickness threshold of either 13 mm or 15 mm. Of the remaining 27 patients, while meeting the diagnostic maximal left ventricular wall thickness threshold for HCM, their medical records unveiled an alternative cause of cardiac hypertrophy. In 4 cases (9%) the hypertrophy was attributed to amyloidosis, and in one case (2%) it was caused by desmoplakin cardiomyopathy. Although these conditions fall within the ESC umbrella definition of HCM, they have their own unique diagnostic codes. Consequently, for the present study, they were considered misregistered despite their inclusion in the broad HCM categorization. If these diseases were to be counted as correctly registered under the diagnostic code of HCM, the PPV would increase to 0.79 (95% CI 0.73–0.84). One patient (2%) had hypertrophy attributed to severe aortic stenosis, one (2%) had coarctatio aortae and one (2%) had dilated cardiomyopathy. For 11 patients (24%) the hypertrophy was

attributed to severe long-standing hypertension. For four patients (9%), left ventricular hypertrophy was attributable to hypertension and aortic valve stenosis. For four patients (9%), our investigations revealed insufficient documentation to conclusively diagnose HCM.

How to Improve the Validity for Research Purposes

We also aimed to identify search criteria that would optimize the PPV of future samples for register-based research from the DNPR. Patients diagnosed in dedicated centers for inherited cardiac diseases were correctly registered in 0.91 (95% CI 0.84–0.95) of the cases, compared to a PPV of 0.52 (95% CI 0.41–0.64) in referral hospitals. Patients that were diagnosed in an outpatient setting were correctly registered in 0.77 (95% CI 0.69–0.84) of the cases, and 0.62 (95% CI 0.45–0.76) in an inpatient setting. The PPV also increased with the number of clinical visits the patient had. Whereas the diagnosis was correct in 0.77 of patients overall, patients with two or more clinical visits were correctly registered in 0.83 (95% CI 0.76–0.88) of the cases increasing with three, four, five or more clinical visits to 0.87 (95% CI 0.81–0.92), 0.90 (95% CI 0.84–0.95), and 0.93 (95% CI 0.85–0.96), respectively. Patients diagnosed before 65 years of age were correctly registered in 0.84 (95% CI 0.75–0.90) of the cases, compared to 0.61 (95% CI 0.49–0.71) correct registrations of patients diagnosed after the age of 65 years. In patients diagnosed in a dedicated center for inherited cardiac diseases and with more than one clinical visit, the PPV increases to 0.99 (95% CI 0.93–1) but these patients constitute only 51% of the total cohort of correctly registered patients. PPV according to patient and clinical settings are presented in Table 2.

The multivariable analysis identified the number of clinical visits registered in the DNPR ($p=0.007$) and the type of hospital ($p<0.001$) as factors significantly affecting the PPV. There was a significant interaction between the number of clinical visits and whether the diagnosis was determined in a dedicated center for inherited cardiac diseases or a referral center. In dedicated centers for inherited cardiac diseases, the number of clinical visits significantly improved the likelihood of meeting the diagnostic criteria ($p=0.02$) whereas in referral hospitals there was no correlation between the number of clinical visits and the likelihood of meeting diagnostic criteria, ($p=0.4$), p for interaction = 0.04.

Variables that affected the PPV but could only be obtained from individual medical records and not from the DNPR included: patients with a pathogenic or likely pathogenic variant, of which 43 of 44 were registered with the correct

Table 2 Validity of the Diagnostic Codes According to Enrichment of the Population with DNPR Derived Data

	All Patients	Correctly Classified	Incorrectly Classified	Positive Predictive Value (95% CI)
All patients	193	148 (77)	45 (23)	0.77 (0.70–0.82)
Female	77 (40)	58 (75)	19 (25)	0.75 (0.65–0.84)
Male	116 (60)	90 (78)	26 (22)	0.78 (0.69–0.84)
Age at time of diagnosis ≥ 65 y	71 (42)	43 (61)	28 (39)	0.61 (0.49–0.71)
Age at time of diagnosis < 65 y	99 (58)	83 (84)	16 (16)	0.84 (0.75–0.90)
Patients with implantable cardioverter-defibrillators	45 (23)	42 (93)	3 (7)	0.93 (0.82–0.98)
Patients without implantable cardioverter-defibrillators	148 (77)	106 (72)	42 (28)	0.72 (0.64–0.78)
Diagnosed at a tertiary center for inherited cardiac diseases	91 (57)	83 (91)	8 (9)	0.91 (0.84–0.95)
Diagnosed in an outpatient setting	127 (78)	98 (77)	29 (23)	0.77 (0.69–0.84)
Two or more physicians determining the diagnose	110 (67)	98 (89)	12 (11)	0.89 (0.82–0.94)
Two or more clinical visits	159 (82)	132 (83)	27 (17)	0.83 (0.76–0.88)
Three or more clinical visits	135 (70)	118 (87)	17 (13)	0.87 (0.81–0.92)

Notes: Data are presented as n (%); due to missing data, the denominator for percentages varies.

Abbreviation: DNPR, Danish National Patient Register.

diagnosis of HCM ($p=0.0005$); performance of a cardiac MRI, which was performed in 41 patients of whom 40 were correctly classified ($p=0.0002$); and left ventricular wall thickness at time of diagnosis (17 mm (IQR 16–19) in the correctly classified versus 15 mm (IQR 12–16) in the incorrectly classified, $p<0.0001$). For 109 patients, two or more physicians were involved in determining the diagnosis, and 0.89 (95% CI 0.82–0.94) of these cases were correctly classified, compared to patients where only a single physician had been involved in the diagnostic work-up, who had a PPV of 0.43 (95% CI 0.3–0.57).

Discussion

We found an overall PPV of 0.77 (95% CI 0.70–0.82) for the diagnosis of HCM in the DNPR. The PPV could be improved by specifying the population using data filters. The PPV was higher in patients diagnosed at a younger age, when more than one clinical visit was registered, and in those where the initial diagnostic work-up was performed in a center with dedicated clinics for inherited cardiac diseases. The PPV was almost perfect (0.99) in patients diagnosed in a center with dedicated clinics for inherited cardiac diseases and with more than one clinical visit but with a loss of sensitivity as these patients constitute only 51% of the total cohort of correct registrations.

Two previous attempts have been made to determine the PPV of HCM.^{11,12} The first study, conducted by Sundbøll et al in 2016, included 20 patients sampled from three hospitals in the Central Denmark Region, which had a catchment area of 1.2 million inhabitants at the time. Of these 20 patients, 18 were correctly identified as having HCM, yielding a PPV of 0.9.

A more recent study by Nielsen et al, validated the referral HCM diagnoses for patients referred with a diagnosis of HCM from regional hospitals to a tertiary University hospital with a dedicated center for inherited cardiac diseases, as opposed to our study that validated discharge- or outpatient diagnoses in the DNPR. The study found that 164 of the 240 patients had their diagnosis confirmed at the tertiary hospital, resulting in a PPV of 0.68.

Our results are in concordance with findings from Sweden where the PPV of HCM diagnostic codes in parts of Sweden have been reported to be 0.68–0.88 in the two studies previously mentioned with 129 and 184 patients, respectively.^{13,14} Previous studies have indicated an overall low PPV of 0.66 in medical diagnoses.⁷ In this regard it is important to mention that a formal threshold for an acceptable PPV has yet to be agreed upon. Nonetheless, a PPV of 0.77 in HCM is an improvement compared to the aforementioned average of medical diagnoses but still falls short of the PPV of 0.9 reported in the prior Danish study.¹¹ Therefore, it is important to acknowledge that if no data filters are used, a significant proportion of patients with a registered HCM diagnosis do not fulfill formal diagnostic criteria.

While certain diseases are encompassed by the broader definition of HCM, such as desmoplakin cardiomyopathy and amyloidosis, these diseases have their own diagnostic codes in the DNPR. Hence, we considered these as misclassifications when the registered diagnosis was HCM. If these diseases were to be counted as correctly registered under the diagnostic code of HCM, the PPV would increase to 0.79 (95% CI 0.73–0.84). Furthermore, if all four patients with uncertain diagnoses, whom we counted as incorrectly registered due to insufficient examination, were instead considered correctly registered, the PPV would rise to 0.79 (95% CI 0.72–0.84).

The PPV of the HCM diagnostic codes increased with the number of clinical visits registered, making the number of clinical visits a potentially useful filter for increasing the number of true positives. Some patients may have initially received the HCM diagnosis as a provisional diagnosis during their first visits, pending further investigations such as MRI, genetic testing, or assessment for amyloid. It is problematic for research purposes that these provisional diagnoses remain in the DNPR. Furthermore, filtering the data for the number of clinical visits would reduce the diagnostic sensitivity as 30 correctly diagnosed patients (20% of the correctly registered) had only one or two clinical visits. Of our sample, 57% were diagnosed in a center with dedicated clinics for inherited cardiac diseases, and of these, 91% were correctly classified compared to 52% correct classification of those diagnosed in a non-specialized setting. Of the 8 patients incorrectly classified in the dedicated centers for inherited cardiac diseases, seven (88%) were first-degree relatives mistakenly registered with a diagnosis of HCM during screening, even if they did not fulfill diagnostic criteria at the time of assessment, which the registers, unfortunately, are unable to filter for. In this regard, it is important to point out that incorrect classification does not equal incorrect treatment.

Clinical parameters such as genetic background, maximal wall thickness, and number of physicians involved in the diagnosis increased the diagnostic accuracy. Albeit improving diagnostic accuracy is of paramount importance, these parameters could only be obtained from individual medical records and not from DNPR registration. The purpose of this study was to validate the HCM diagnosis in the DNPR and to identify factors that would increase or decrease the PPV, which could improve future register-based research's ability to sample true positive HCM patients.

A strength of this study was that the sample size was considerably larger and collected more data on the individual patients compared to a previous Danish attempt to validate the diagnostic codes from DNPR. A limitation of the study is that our data extraction did not allow us to differentiate between the two diagnostic codes of HCM and obstructive HCM. Therefore, we calculated a PPV based on both diagnostic codes and not individually. Our sample comprised of patients from the Eastern regions of Denmark, covering approximately 44% (2.6 million/5.9 million inhabitants) of the Danish population. The Danish population is homogenous across all regions, there is universal access to free healthcare, and national guidelines and nationwide collaboration, including a national pedigree database for use in family screening, advocate the same management of patients across hospitals and regions.¹⁶ Therefore, we consider the sample representative of a national setting. The median age of our random sample was 61 years (IQR 50–70). In a contemporary nationwide study of patients with HCM, the mean age was 63.1 (IQR 52.1–72.1) at diagnosis, corroborating the representativeness of our cohort.¹⁷

It must also be acknowledged that images from original echocardiograms could not be accessed and reviewed for all patients for whom echocardiography reports were available.

Conclusion

The overall PPV of the combined non-obstructive HCM and obstructive HCM diagnostic codes in a random sample of the DNPR was 0.77 (95% CI 0.70–0.82). The random sample was representative of a nationwide HCM population regarding age at diagnosis and was overall considered representative based on a homogenous Danish population across regions. The validity of the diagnosis was higher at centers with dedicated clinics for inherited cardiac diseases indicating potential variations in the application of diagnostic criteria across different centers. These findings may prove useful for future register-based research.

Abbreviations

CI, Confidence interval; DNPR, Danish National Patient Register; ESC, European Society of Cardiology; HCM, Hypertrophic cardiomyopathy; ICD, International Statistical Classification of Diseases and Related Health Problems; IQR, Interquartile range; MRI, Magnetic resonance imaging; PPV, Positive predictive value.

Disclosure

Dr Jens Jakob Thune reports personal fees from Astra-Zeneca, personal fees from Bristol Myers Squibb, outside the submitted work. The authors report no conflicts of interest in this work.

References

1. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA*. 2002;287(10):1308–1320. doi:10.1001/jama.287.10.1308
2. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation*. 2020;142. doi:10.1161/CIR.0000000000000937
3. Arbelo E, Protonotarios A, Gimeno JR, et al. 2023 ESC guidelines for the management of cardiomyopathies: developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC). *Eur Heart J*. 2023;44(37). doi:10.1093/eurheartj/ehad194
4. Maron BJ, Spirito P, Roman MJ, et al. Prevalence of hypertrophic cardiomyopathy in a population-based sample of American Indians aged 51 to 77 years (the strong heart study). *Am J Cardiol*. 2004;93(12):1510–1514. doi:10.1016/j.amjcard.2004.03.007
5. Zou Y, Song L, Wang Z, et al. Prevalence of idiopathic hypertrophic cardiomyopathy in China: a population-based echocardiographic analysis of 8080 adults. *Am J Med*. 2004;116(1):14–18. doi:10.1016/j.amjmed.2003.05.009
6. Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults. Echocardiographic analysis of 4111 subjects in the CARDIA study. Coronary artery risk development in (young) adults. *Circulation*. 1995;92(4):785–789. doi:10.1161/01.cir.92.4.785

7. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish national patient registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449–490. doi:10.2147/CLEP.S91125
8. Delekta J, Hansen SM, Alzuhairi KS, Bork CS, Joensen AM. The validity of the diagnosis of heart failure (I50.0–i50.9) in the Danish national patient register. *Dan Med J*. 2018;65(4):A5470.
9. Coloma PM, Valkhoff VE, Mazzaglia G, et al. Identification of acute myocardial infarction from electronic healthcare records using different disease coding systems: a validation study in three European countries. *BMJ Open*. 2013;3(6):e002862. doi:10.1136/bmjopen-2013-002862
10. Joensen AM, Jensen MK, Overvad K, et al. Predictive values of acute coronary syndrome discharge diagnoses differed in the Danish national patient registry. *J Clin Epidemiol*. 2009;62(2):188–194. doi:10.1016/j.jclinepi.2008.03.005
11. Sundbøll J, Adelborg K, Munch T, et al. Positive predictive value of cardiovascular diagnoses in the Danish national patient registry: a validation study. *BMJ Open*. 2016;6(11):e012832. doi:10.1136/BMJOPEN-2016-012832
12. Nielsen SK, Rasmussen TB, Hey TM, Zaremba T, Lassen JF, Mogensen J. Frequency of misdiagnosis in hypertrophic cardiomyopathy. *Eur Heart J Qual Care Clin Outcomes*. Published online April 25, 2024. doi:10.1093/ehjqcco/qcae031
13. Magnusson P, Palm A, Branden E, Möner S. Misclassification of hypertrophic cardiomyopathy: validation of diagnostic codes. *Clin Epidemiol*. 2017;9:403–410. doi:10.2147/CLEP.S139300
14. Basic C, Rosengren A, Lindström S, Schauffelberger M. High validity of cardiomyopathy diagnoses in western Sweden (1989–2009). *ESC Heart Fail*. 2018;5(2):233–240. doi:10.1002/ehf2.12224
15. Wilson EB. Probable inference, the law of succession, and statistical inference. *J Am Stat Assoc*. 1927;22(158):209. doi:10.2307/2276774
16. Henriksen DP, Rasmussen L, Hansen MR, Hallas J, Pottegård A. Comparison of the five Danish regions regarding demographic characteristics, healthcare utilization, and medication use—a descriptive cross-sectional study. *PLoS One*. 2015;10(10):e0140197. doi:10.1371/journal.pone.0140197
17. Jacobsen MHB, Petersen JK, Modin D, et al. Long term mortality in patients with hypertrophic cardiomyopathy—a Danish nationwide study. *Am Heart J Plus*. 2023;25:100244. doi:10.1016/j.ahjo.2022.100244

Clinical Epidemiology

Dovepress

Publish your work in this journal

Clinical Epidemiology is an international, peer-reviewed, open access, online journal focusing on disease and drug epidemiology, identification of risk factors and screening procedures to develop optimal preventative initiatives and programs. Specific topics include: diagnosis, prognosis, treatment, screening, prevention, risk factor modification, systematic reviews, risk & safety of medical interventions, epidemiology & biostatistical methods, and evaluation of guidelines, translational medicine, health policies & economic evaluations. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use.

Submit your manuscript here: <https://www.dovepress.com/clinical-epidemiology-journal>