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Evaluation of natriuretic peptide recommendations in heart failure clinical practice guidelines☆

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ABSTRACT

Background: The B-type naturietic peptides (NPs) are associated with heart failure (HF). This investigation was designed to evaluate heart failure clinical practice guideline (CPG) recommendations for the use of NPs.

Methods: A search for English language CPGs for HF published since 2011 was conducted. A search for systematic reviews (SR) and meta-analysis for NPs in HF was conducted for the years 2004–2012. Each HF CPG was evaluated by two independent reviewers. Key recommendations for NPs and the supporting references were abstracted. The key findings from each SR were abstracted.

Results: Seven English language HF CPGs were found, all of which made recommendations for the use of NPs in diagnosis. Four made recommendations for prognosis and three for management. The European CPG scored highly for rigor of development with the Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) while the others did not. North American CPGs made stronger recommendations citing higher grades of evidence for the use of NPs in HF than the European or Australian CPGs. The CPGs mostly cited primary studies 47/66 to support the recommendations. From twelve available SRs, five were cited by CPGs. One CPG conducted a SR.

Conclusions: The SR evidence to support NP use in CPGs has not been well cited in the CPGs and the recommendations are only partially supported by the SR evidence. Future CPGs should consider improving the methodology used to evaluate laboratory tests.

1. Introduction

Clinical practice guidelines (CPGs) are produced to facilitate incorporation of evidence into clinical practice. With a wider acceptance of natriuretic peptides (NPs) as an important part of the pathogenesis in heart failure (HF), they have been included in a number of clinical practice guidelines.

CPGs guidelines follow a methodology to: set questions; collect and evaluate the evidence they present; and rank the guidance offered. Systematic review (SR) of the available evidence is an important part of guideline development and is listed as a standard by the Institute of Medicine, which should be met by guideline writers [1]. SRs consider the body of available evidence with critical appraisal in way that minimizes bias and random error. Thus a well conducted SR is more likely to estimate the true effect of an intervention than individual studies. There is a role for recent well conducted individual studies to be considered in guideline development in an effort to reflect the most current literature. In a typical evidence hierarchy, SR of randomized controlled trial (RCT) data would be seen as a higher level of evidence than individual RCTs, and SR of non-randomized studies considered a higher level of evidence than the individual non-randomized studies. RCT for evaluation of diagnostic laboratory tests are not common and thus the evidence is often based on non-randomized studies [2]. The Centre for Evidence Based Medicine (CEBM) has a table describing the different types of evidence available and how these could be ranked for different purposes including diagnosis and prognosis [3].

The Appraisal of Guidelines for Research & Evaluation Instrument (AGREE II) is widely used appraisal tool for guidelines, and has been validated for use in both clinical and laboratory medicine guidelines [4,5]. Guidelines in cardiology have been criticized for not meeting the AGREE II criteria [6]. Methodological quality was noted to be one of the weaker aspects of guidelines in cardiology. Consideration of the best available body of evidence is an important component of methodological rigor. For medical tests included in CPGs a list of important factors for consideration has been proposed [7]. This list has been used to evaluate a number of CPGs but has not yet been adopted on a wide basis.

Abbreviations: CPG, clinical practice guideline; NP, B-type natriuretic peptide; HF, heart failure; SR, systematic review; RCT, randomized controlled trial; CEBM, Centre for Evidence Based Medicine; AGREE II, Appraisal of Guidelines for Research and Evaluation Instrument; AHRQ, Agency for Healthcare Research and Quality; IOM, Institute of Medicine.

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A number of systematic reviews have considered NPs in the setting of their research question in HF [8]. The systematic reviews have demonstrated that NPs have clinical utility, particularly in excluding HF, as NPs have excellent negative predictive value for HF. Given that there is a strong body of evidence for NPs in HF evaluated by SR, the recommended use of NPs should be consistent between different guidelines asking the same question and should be consistent with the SR literature on the topic.

This study investigates the question of whether the current HF CPGs use the highest available level of evidence to support the recommendations for NP use. To answer this question, this study critically evaluates the recommendations for use of NPs reported in HF CPGs. This was achieved by identifying CPG recommendations, evaluating the quality of the CPGs, identifying the evidence supporting CPG recommendations for NPs and evaluating the reporting of laboratory factors related to the recommendations.

2. Methods

2.1. Clinical practice guideline

A search for clinical practice guidelines for heart failure was undertaken using PubMed, EMBASE, Medline, Cochrane database, the National Institute for Clinical Excellence website, the Scottish Intercollegiate Guideline Network and the Guideline Clearing House in Jan 2015. Search terms used were 'guidelines' and 'heart failure'. Guidelines published since 2011 were included. Guideline documents that were not supported by a specialty society were excluded. Guidelines that commented on the appropriateness of another guideline or that represented a published guideline were excluded. All published guidelines found by literature search were cross-referenced with the associated society webpage to ensure it represented the most current version of the guideline. The most current version was used for the evaluation.

Guidelines were searched for 'BNP' 'NTpro-BNP' and 'natriuretic peptide' to identify sections which include recommendations about the use of NPs. The recommendations were abstracted from each guideline by one reviewer and independently checked for accuracy by a second reviewer. Disagreements between reviewers were resolved by discussion. Each recommendation was categorized as being for the diagnosis, prognosis, or guiding therapy for heart failure. The evidence ranking system for each CPG was reviewed and the grading of the evidence for each CPG recommendation recorded. The references cited for each CPG recommendation were tabulated to record the type of study and checked against the published data tables in the Agency for Healthcare Research and Quality (AHRQ) comparative effectiveness reviews [9,10].

The section(s) of each guideline related to each recommendation were reviewed by two independent reviewers using the AGREE II tool [4]. Each CPG was assessed using a checklist of pre-analytical, analytical, and post-analytical factors which was developed from the work of Aakre et al. [7]. This comprehensive checklist has been endorsed by the Working Group on Guidelines of the European Federation of Clinical Chemistry and Laboratory Medicine as a framework for developing and evaluating recommendations for all laboratory tests included in a clinical practice guidelines. The checklist was modified by the authors of this study for use in evaluating recommendations for the use of NPs in HF by selecting those items analytically relevant to NPs.

2.2. Systematic review evidence

A search for systematic reviews and meta-analyses for NP in the diagnosis, prognosis, or therapy of HF was conducted to include any SR that would have been available to the CPGs. The end date for this search was Dec 2012 as this publication date would have allowed for consideration by most of the CPG writing groups. PubMed, EMBASE, Medline, the Cochrane data base and the AHRQ data base were searched for articles in English published between 2004 and 2012 search terms included 'BNP', 'NTpro-BNP', or 'natriuretic peptide' and 'heart failure', 'review' and 'meta-analysis'. Each abstract found in the search was considered and the paper was included if it was a systematic review, with or without meta-analysis, on the question of the use of NPs in one or more of the diagnosis, prognosis, or management of HF. Meta-analysis performed on studies not selected by systematic searching were excluded. The SRs found were cross referenced against the reference list of each CPG and the number of times each SR was cited by a CPG was recorded.

3. Results

3.1. Clinical practice guidelines for heart failure

Seven CPGs were included once duplicates, guidelines published prior to 2011 and guidelines that met exclusion criteria [11–13] were excluded. The included CPGs were published by the Canadian Cardiovascular Society (CCS) [14], the American College of Cardiology/American Heart Association (AHA) [15], the European Society of Cardiology (ESC) [16], the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (ANZ) [17], National Institute for Health and Care Excellence (NICE) [18], Institute for Clinical Systems Improvement (ICSI) [19], and the Japanese Circulation Society (JCS) [20].

All of the CPGs made recommendations for the use of NPs in diagnosis, four for prognosis and three for guiding therapy. A total of 19 recommendations were made. The recommendations made and the corresponding strength of recommendation and level of evidence as reported in each guideline are shown in Table 1. North American CPGs made stronger recommendations citing higher grades of evidence for the use of NPs in HF than the other CPGs. The CPGs mostly cited primary studies that were not RCTs. Both systematic and narrative reviews were also cited. Fig. 1 shows the types of studies cited by each CPG for the recommendations made in the three areas. Fig. 2 demonstrates that the date of publication of primary papers and reviews does not differ. The NICE CPG [18] performed an internal SR and was not included in Figs. 1 and 2 as it cited primary papers but used a SR approach to grade the recommendations.

3.2. Quality of the clinical practice guideline with respect to the laboratory testing

The AGREE II evaluation (Table 2) found that Domain 3 (rigor of development) had scores ranging from 32% to 98%. Question 12 from domain 3 "there is an explicit link between the recommendations and the supporting evidence" was scored less than 5/7 for all the CPGs with the exception of ESC and NICE. The important pre-analytical, analytical, and post-analytical considerations for NP testing as measured by the medical test checklist are reported in Table 3 and demonstrate variability (12%–57%) in the number of included factors between CPGs.

3.3. Systematic reviews for use of NPs in heart failure

Seven SRs regarding NPs in diagnosis of HF were identified [21–27] two in prognosis in HF population [28,29], and three in the guiding therapy for HF [30–32] (Table 4). The CPGs vary in how they use the SRs. (Table 1 and Fig. 1). Of the twelve available SRs, five were cited [23,24,26,31,32].

4. Discussion

4.1. Highest level of evidence

The most interesting finding in this study is the lack of consideration for published SR by the CPG writers. The use of SR is one of the standards