Short Communication

Identifying Research Gaps in the Diagnosis and Treatment of Hypertension: Evidence from a Guideline Update

Abstract

Background: The development of clinical practice guidelines presents a unique opportunity to identify research gaps systematically. This study aimed to uncover such gaps in the hypertension field while updating the Iranian hypertension guideline. **Materials and Methods:** This study was conducted as part of the systematic review component of the 2021 Iranian hypertension guideline update. An extensive search of electronic databases was performed to identify evidence relevant to PICO (Population, Interventions, Comparisons, Outcomes) questions. Any topic without evidence with high certainty of effect was considered a knowledge gap. **Results:** A total of 227 studies were reviewed and appraised. Nine topics, such as non-pharmacological treatment, treatment thresholds, visit and follow-up intervals, laboratory tests, drug immunotherapy, adherence to treatment, complementary medicine, telehealth, COVID-19 were identified as research gaps. **Conclusions:** The identified research gaps can be examined and prioritized by policymakers in the research field, and actions can be taken to plan for addressing them.

Keywords: *Evidence gaps, hypertension, practice guideline*

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Introduction

A research gap represents a deficiency in the existing body of knowledge that limits researchers' ability to answer a particular question. Identifying and prioritizing these gaps is critical to any research agenda.[1]

Hypertension, a significant global health concern, is a primary risk factor for disability and mortality, particularly from cardiovascular diseases.[2] However, hypertension is preventable and manageable, and its treatment relies heavily on accurate and up-to-date clinical practice guidelines.[3]

Guideline development committees are uniquely positioned to identify research gaps.[1] When developing guidelines, committees systematically review the available evidence, recognizing its strengths and limitations. Given the limited research on identifying research gaps, the evidence synthesized in guideline development processes offers a valuable resource for uncovering areas in need of needing further study.[1,4,5] Previous studies have reported identifying of research gaps during guideline development.[1,6,7] However, due to the limited development and updating of national guidelines and the variability of Population, Interventions, Comparisons, Outcomes (PICO) questions across different guidelines, this study aimed to identify research gaps in hypertension concurrently with the systematic update of the Iranian hypertension guideline.

Materials and Methods

This article results from a systematic review conducted in the process of updating the Iranian Hypertension Guidelines in 2021.[8,9] The guideline update process adhered to rigorous standards and was guided by established methodologies. Initially, a guideline development group was formed, and the scope of the updated guideline (domain, target group, and audience) was defined. PICO questions were formulated for to the study population, proposed intervention, comparator intervention, and outcomes.[4,5] These questions guided the systematic review conducted by the Systematic Review Group (SRG).

The SRG systematically searched for hypertension guidelines, systematic reviews, and meta-analyses published between 2015

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and 2021. Databases, including MEDLINE via PubMed, Embase, Scopus, Web of Sciences, Cochrane Library, and Google Scholar, were searched using subject- and keyword-based strategies. If the search for systematic reviews and meta-analyses was unsuccessful, a new systematic review was conducted to answer the PICO question.

If evidence for a specific question or part thereof (e.g., for certain outcomes or subgroups) was either absent or scored low in the evidence grading process, this was reported as a knowledge gap to the guideline update group.[4,10] Evidence grading considered factors such as the type, number, and quality of studies; risk of bias, consistency of results, directness of evidence related to the intervention and health outcomes, precision of effect estimates, strength of association, and publication bias. A "high" grade indicated a high confidence level that the evidence reflected the actual effect and that further research was unlikely to change confidence in the effect estimate. A "moderate" grade indicated moderate confidence, while a "low" grade indicated low confidence. A "very low" grade signified that the evidence was either unavailable or insufficient to conclude.[10]

Ethical considerations

The authors declare that they have avoided plagiarism and redundant publication. They have never manipulated the data for their own benefit. The results of the analysis were completely honest.

In the current study, ethical principles have been considered, and maximum care was taken to avoid any kind of bias in analyzing the data of retrieved from articles.

Results

An initial search yielded 33,975 studies addressing the PICO questions. After excluding duplicates, irrelevant studies, those without full text, and those not published in English or Persian, 227 studies, including systematic reviews, meta-analyses, and in some cases, cohort studies and randomized controlled trials (RCTs), were included for evidence review and appraisal.

Based on the evidence identified and its grading, several research gaps were identified and are listed in Table 1.

Discussion

In the PICO question related to the first-line treatment for patients with pre-hypertension and hypertension, lifestyle modification was considered as the intervention. Although lifestyle modification is an effective non-pharmacological treatment for hypertension, the systematic review results indicated that there were insufficient studies in this area or that they were of a low level in the evidence ranking. The results of a systematic review in the Asia-Pacific region on primary prevention through lifestyle modification also showed a considerable information gap and no high-quality cost-effectiveness studies in this area.[11]

Our findings revealed significant gaps in the literature, particularly regarding specific outcomes and certain subgroups.

Clark and colleagues found in their assessment of over 2500 Cochrane reviews, that 82% of Cochrane

Table 1: Research gaps (Knowledge gaps) in hypertension management

Subject	Description
Non-pharmacological treatment and the effect of a healthy lifestyle on hypertension	The effect of exercise, nutrition, alcohol, smoking, stress, etc., on hypertension
Thresholds for determining treatment initiation and goals for achieving hypertension control	The threshold for starting pharmacological treatment in patients with high blood pressure and sub-groups of chronic kidney disease, diabetes and patients with heart and vascular diseases and the elderly, as well as the consequences of dementia and side effects related to treatment
Visit intervals and follow-up of hypertensive patients	Appropriate visit intervals in patients with hypertension before and after reaching the treatment goal
Laboratory tests to determine the initiation of treatment	Necessary tests about reducing costs and improving results and their intervals
Drug monotherapy versus combined drug therapy	Review of long-term data comparing two treatment regimens in reducing clinical outcomes, such as reduction of MACE (Major adverse cardiac events), mortality, dementia, and adverse effects, and health economic analyses of cost-effectiveness and budget implications for two treatment regimens.
Adherence to treatment	Time, frequency, and intensity of interventions that improve adherence to treatment Time, frequency, and intensity of interventions that improve adherence to treatment
Covid-19	Covid-19 and high blood pressure, blood pressure fluctuations in people with hypertension after contracting Covid or hypertension as one of the long-term complications of Covid or symptoms of PCC syndrome
Complementary medicine	The effect of various complementary medicine methods on high blood pressure and related outcomes
The role of telehealth in hypertension control	Effectiveness of telemonitoring for patients with Hypertension (HTN) and long-term outcomes or its generalizability to patients with different backgrounds and educational levels

evidence, included a recommendation for a specific type of intervention. However, only 17% of the documentation specified the intervention performed, the study population, and the outcomes of the interventions. Furthermore, 12% did not identify these three components.[12] This result could be due to a lack of clarity in the key PICO question posed by the design team. The PICO question must be well-defined to guide the systematic review team in articulating what research is needed and why.[4]

The frequency of visits and follow-up of patients with hypertension is also essential. While shorter follow-up intervals lead to adverse outcomes such as an increased treatment burden for patients and the national health system, they improve adherence to treatment and control of blood pressure and make monitoring adverse effects more feasible.[13,14] However, no evidence with high certainty of effect was found in this regard, nor was it regarding the cost, resources, and cost-effectiveness of reducing or increasing follow-up intervals. However, reducing the frequency of visits for older adults appears cost-effective.[15]

A review of studies on laboratory tests could not clearly and precisely determine the frequency of performing tests. In low-resource settings, the need to perform laboratory tests before starting treatment can hinder treatment and create inequalities.[16] The cost of performing tests for an individual is relatively insignificant compared to the lifelong treatment costs and complications. However, due to the high prevalence of hypertension in most communities, performing tests has a significant impact on the health system.[17]

New systematic reviews and long-term comparative data are needed to compare monotherapy and combination therapy regimens. More recent studies have mainly compared of patient adherence to these two treatment regimens, which has been higher in the combination therapy group.[18]

From the patients' perspective, numerous individual and social factors influence treatment adherence, such as lack of family support, local facilities, and medication availability.[19] The results of a systematic review showed that simplifying drug regimens for patients can increase their treatment adherence by 6% to 20%.[20]

Remote health strategies such as telemedicine, eHealth, and mobile health technologies are new and innovative tools that facilitate the management of hypertensive patients.[21]

Although the overall certainty of the evidence found for the positive impact of using remote health strategies on blood pressure control was high, and many beneficial effects (such as reducing Systole Blood Pressure (SBP) and Diastole Blood Pressure (DBP) throughout the day in populations with hypertension and cardiovascular disease, improving quality of life) were reported for various types of these strategies,[22] despite the existing evidence, there was no empirical evidence of long-term outcomes or generalizability to patients with different backgrounds and educational levels regarding the effectiveness of remote monitoring for patients with HTN.[23]

Conclusion

Based on the results, it is recommended that planning be done to review and prioritize the identified research topics and announce the results to relevant organizations to address the existing research gaps.

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Conflicts of interest

Nothing to declare.

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