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Improving diagnosis of primary aldosteronism through education: a modified Delphi study to identify key learning points

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Abstract

Background: Primary aldosteronism (PA) is the most common endocrine cause of secondary hypertension and can be effectively managed, or even cured, with targeted treatment. Despite this, it remains largely undiagnosed leaving a significant patient population with resistant hypertension and modifiable cardiovascular risk.

Objective: To determine expert consensus on key information about PA that should ideally be taught to medical students as a step toward improving the detection of this common, underdiagnosed, and often easily treated condition.

Design: The study employed a modified Delphi method which consisted of three rounds, the first of which contained an open-ended question about key areas that experts believe to be most important for inclusion in medical teaching resources and then progressing to assessment of individual versus group rankings of consensus items. Experts included both clinician-educator-researchers and patients with lived experience.

Results: Nine critical knowledge areas in epidemiology, diagnostics, and pathophysiology were identified by the Delphi as consensus items, with the highest ranked being: "PA is common but often under-diagnosed – think about it with every hypertensive patient." **Conclusion:** Experts reached a consensus, for the first time, on nine critical knowledge areas about PA that should be covered in medical education. Importantly, the consensus accounted for patients' values and decisions. The results of this study could be used to assess medical student knowledge and their learning resources to facilitate curriculum development and medical resource updates to ensure the timely and accurate diagnosis of PA in hypertensive patients.

Keywords: Conn's syndrome, Delphi method, endocrinology, hyperaldosteronism, hypertension, medical education, primary aldosteronism

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Introduction

Hypertension is the leading cause of cardiovascular disease and the largest preventable risk factor for overall mortality,¹ with up to 22.8% of Australian adults recording blood pressure (BP) measurements over 140/90 mmHg.² The poor control is partly attributable to unrecognized primary aldosteronism (PA), the most common endocrine cause of secondary hypertension, accounting for 5%–15%³ of hypertension in primary care and up to 30% in those with resistant hypertension.^{4–6}

While experts recognize PA as a common cause of hypertension, previous literature has described PA as a rare disease accounting for less than 1%

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of hypertensive patients,^{4,5} and at present it remains grossly underdiagnosed in clinical practice.⁷ A study of 4660 individuals with resistant hypertension found that only 2.1% were screened for PA despite all of them fulfilling screening criteria.⁵ This has significant implications for patients as untreated PA is associated with increased morbidity and reduced quality of life^{8,9} secondary to cardiovascular, renal, and metabolic consequences.^{10–12}

Poor diagnostic rates are a product of multiple factors including inadequate understanding and acknowledgment of PA. Educating medical students is one component of a multi-pronged approach to ensure increased awareness and improved diagnosis and treatment of PA. Targeted PA teaching during medical training is important as teaching implemented during initial training can have a significant impact on future physician clinical reasoning and diagnostic patterns¹³ and may also play a crucial role in improving patient outcomes.

The lack of consensus on what to teach medical students about PA is a critical gap that contributes to deficient knowledge and subsequent underdiagnosis of a common condition. Medical school curricula are prone to overcrowding and, due to continually expanding medical knowledge, face constant pressure from various disciplines to include more content and more detail about more things.¹⁴ A good argument can be made to focus on prevalent and treatable conditions as such knowledge is likely to positively impact patients' health. Now that the prevalence and treatment for PA are better understood, the degree of attention on this disease in medical schools may warrant review.

Hence, we sought to determine key, up-to-date, knowledge areas about PA that experts believe are most important for medical students to learn. The expert consensus will be invaluable for medical curriculum development. It can also be used to assess whether medical professionals in training have adequate knowledge and whether their learning or teaching resources contain adequate information as determined by experts in PA.

Method and participant

A modified three-round Delphi survey was performed with an international panel, composed of both clinicians with expertise in PA and patients with PA. The Delphi method is a consensusbased iterative process that uses repetitive questionnaires to gather information from a selected panel.¹⁵

The initial Delphi method was first implemented in the 1960s by Dalkey and Helmer to define and predict military priorities.¹⁶ This method has since been refined, from which a conventional Delphi is defined by its ability to utilize anonymity and controlled feedback to assess initial judgments and make alterations to determine panel consensus.¹⁷

The current study employed a modified Delphi method which consisted of three rounds, the first of which contained an open-ended question about key areas that experts believe to be most important for inclusion in medical teaching resources and then progressed to assessment of individual versus group rankings of PA consensus items (Figure 1). The questionnaires were developed and distributed through Google Forms. The link and instructions to these questionnaires were provided to panel members through email.

Panel

Panel participants (other than consumers) were selected for their clinical expertise in managing PA as well as active involvement in research and education. They were also chosen for diverse geographic representation with expertise across Australia, America, Asia, and Europe. All invited panel members accepted the invitation and completed all three stages of the Delphi process.

The consumer panel participants were selected for their advocacy for all individuals with PA through the establishment of the Primary Aldosteronism Foundation and the Conn's Syndrome/Hyperaldosteronism Support Group. Their lived experience of PA (encompassing both bilateral and unilateral forms) and related comorbidities, including obstructive sleep apnea and atrial fibrillation, are supplemented by extensive consumer feedback via these advocacy platforms. They engage with 200–1500 individuals per month via these platforms.

Written consent was obtained from all panel participants (clinicians and consumers) for their involvement and contributions to this Delphi study.



Figure 1. Modified Delphi method.

Round 1

The objective of Round 1 was to confirm panel member involvement with PA research, patient care, and student teaching; alongside identifying aspects of PA that they believe to be most important in medical student teaching.

Questions included in Round 1

- Are you a PA clinician or patient?
- How many years have you been involved in the management of patients with PA?
- Approximately how many patients with PA (new and reviews) do you currently see per month?
- Are you involved in teaching medical students?
- Are you involved in research on the topic of PA?
- Do you currently teach students about PA?
- Based on your expertise, what do you believe to be the three most important messages about PA that should be taught to medical students by the time they graduate? Please rank them in the order of importance and provide a short justification for each as to why you believe it to be an important aspect of PA knowledge for medical students.

The final question was used as the primary resource with responses grouped into similar categories and then redistributed to the original panel for calibration and assessment of consensus via survey 2.

The responses to the final question were collated and grouped into key teaching points according to their similarity. Points identified as important by more than one panel member were deemed consensus items and redistributed to the original panel for calibration and assessment of consensus in Round 2.

Round 2

The aspects of PA identified as consensus items were redistributed to the original panel members who were asked to rank them in order of importance from most important to least important.

The mean and median were calculated from the responses of the entire panel (13 participants), patients only (2), and clinicians only (11). A distinction was made to identify whether there was a significant variance between aspects of PA that clinicians versus patients believed to be most important.

Round 3

The responses from survey 2 were compiled to generate an ordered ranking of the previously identified critical knowledge areas of PA. The group ranking was redistributed to panel members alongside their own ranking, from which panelists were allowed to change their initial ranking after comparison to the group ranking.

Results

Round 1

Response to Round 1 of the Delphi confirmed the clinical expertise of the clinician panel members. They have an average of 16 years of experience with PA management, seeing an average of 19 patients with PA per month. They were all involved in PA research and 9/10 were involved with medical student teaching.

The two patients were actively involved in consumer advocacy as founding members of the PA Foundation (based in Arizona) or Conn's Syndrome/ Hyperaldosteronism Patient Support Group (with 4000 members on Facebook). One of them endured 25 years of unmanaged hypertension with associated hypertensive crises before being diagnosed with bilateral adrenal hyperplasia and commencing medical management with mineralocorticoid receptor antagonists. The other patient was initially diagnosed with an aldosterone-producing adenoma and underwent an adrenalectomy prior to discovering he also had bilateral disease which was then treated with a mineralocorticoid receptor antagonist.

Round 1 also identified nine critical knowledge areas about PA encompassing prevalence, symptoms, diagnostic methods, pathophysiology, treatment methods, and associated risks. Responses were assigned points based on the ranking provided by the panel, that is, most important allocated three points, the second most important two points, third most important one point (Table 1).

Round 2

A ranking of the points identified from Round 1 was established in Round 2 of this Delphi. Significant variation between groups was not identified; however, some variance was noted between responses from patients and clinicians. The patients gave greater weight to teaching about the spectrum of PA severity and screening all hypertensive patients for PA (Table 2).

Round 3

The responses from the third survey were closely aligned with the ranking achieved in Round 2 despite 11 members altering their rankings between Rounds 2 and 3. The only difference was a new distinction between points 4 (ARR is a key screening test) and 5 (pathophysiology of PA) which were initially equal in both mean and median (Table 3).

Discussion

This modified Delphi process identified nine consensus knowledge areas considered by both clinicians and patients with expertise in PA as crucial for medical students to understand.

In addition to inviting clinicians and researchers to join the expert panel, we actively recruited patients because they carry a similar goal to healthcare professionals in seeking optimal treatment for themselves and others with equivalent chronic conditions.¹⁸ They provide a unique perspective about areas of care, including "impact, the practicalities of treatment, and the attitudes of other people, including the medical profession, to [their] condition."¹⁹ In this circumstance, their involvement allows for a holistic perspective with greater insight into patient experience and allows for emphasis on patient-centered models of care in the continuing development of medical education.

Consensus points that held greatest importance across the panel focused on epidemiological knowledge and the implication of late diagnosis of PA on patient morbidity.

While all nine key knowledge areas identified are relevant to PA and medical education, the top three points and their relevance in current literature are discussed below.

Key knowledge area 1: PA is common but underdiagnosed, think about it with every hypertensive patient

Various studies have demonstrated the high prevalence of PA in patients with resistant hypertension as well as those presenting in primary care

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Responses	Frequency	First importance (3)	Second importance (2)	Third importance (1)	Total
PA epidemiology – prevalence in hypertensive patients (underdiagnosed and underrecognized)	8.5	8.5			25.5
Increased cardiovascular, renal, and metabolic risk compared to essential matched HTN	5		3	2	8
Testing in initial hypertension assessment	3.5	1	2	0.5	7.5
PA screening (screening guidelines)	2.5	2		0.5	6.5
PA screening methods	3		2	1	5
Pathophysiology of condition	1.5	0.5	1		3.5
Spectrum of condition, not binary	2		1	1	3
Hypokalemia is not always present	2		1	1	3
Treatment options	2			2	2
PA subtypes	1		1		2
inadequacy of current screening for aldosterone levels (aldosterone blood concentration)	1			1	1
PA Symptoms and signs aside from resistant hypertension	1		1		2
Education of spironolactone prescribing	1			1	1
Condition not fully understood: limitation of current disease	1			1	1
Cardiovascular management in PA patients	1			1	1

Table 1. Delphi Round 1 results.

facilities. The exact statistics vary across studies, with prevalence estimates of 4%, 5.9%, and 14% in primary care centers in China, Italy, and Australia respectively,^{10,20,21} and 11%–22% in populations with resistant hypertension.^{22,23} However, the proportion of patients who are screened or diagnosed is much lower, with <1% of eligible hypertensive patients screened in a

Canadian population of more than 245,000 patients identified with resistant hypertension²⁴ and <0.1% of hypertensive patients having the diagnosis of PA in an Australian primary care setting.⁷

These studies support the universal screening of PA in people with hypertension. However, there

Table 2. Delphi Round 2 results.

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Key message	Consensus item	Entire panel		Only clinicians		Only patients		
		Total	Mean	Median	Mean	Median	Mean	Median
Epidemiology	PA is common but underdiagnosed – think about it with every hypertensive patient	17	1.55	1.00	1.50	1.00	1.00	1.00
Increased morbidity	Untreated PA is associated with increased cardiovascular, renal, and metabolic risk when compared to blood pressure- matched essential hypertension	44	4.00	3.50	3.70	3.50	3.50	3.50
Early screening	It is important to test for PA following a diagnosis of hypertension, by measuring aldosterone and renin	51	4.64	4.00	4.60	4.50	2.50	2.50
Screening methods	The ARR is the key screening blood test for PA, however, it is important to recognize that results may be inaccurate due to interfering medications	59	5.36	5.50	4.90	5.50	5.00	5.00
Pathophysiology	Pathophysiology: PA is an adrenal disease characterized by inappropriately high and autonomous aldosterone production and suppressed renin	59	5.36	5.50	4.70	5.00	6.00	6.00
Treatment	PA has targeted treatment or potential cure	68	6.18	5.00	5.50	5.00	6.50	6.50
Hypokalemia presence	Hypokalemia is not always present in PA	70	6.36	5.50	5.70	5.00	6.50	6.50
Spectrum of condition	Spectrum of condition: PA can range in severity	77	7.00	7.50	6.60	7.50	5.50	5.50
Screening guidelines	There are screening guidelines for PA as set out by the Endocrine Society	95	8.64	8.00	7.80	8.00	8.50	8.50
ARR, aldosterone:renin ratio; PA, primary aldosteronism.								

are high-risk patient groups that warrant specific attention, as recommended by the 2016 Endocrine Society Clinical Practice Guideline²⁵:

- Sustained BP above 150/100 mmHg on each of three measurements obtained on different days, or
- Hypertension (BP >140/90 mmHg) resistant to three conventional antihypertensive drugs (including a diuretic), or
- Controlled BP (<140/90 mmHg) on four or more antihypertensive medications
- Hypertension and spontaneous or diureticinduced hypokalemia

- Hypertension and adrenal incidentaloma
- Hypertension and sleep apnea
- Hypertension and a family history of earlyonset hypertension or cerebrovascular accident at a young age (<40 years)
- All hypertensive first-degree relatives of a patient with PA

At present, screening rates are low even in these high-risk groups, with 1%-3% tested despite having resistant hypertension or hypokalemia.^{26–29}

The wide chasm between the expected prevalence and actual screening and detection rates

Table 3. Delphi Round 3 results.

Rank	Key message		Total	Mean	Median		
1	Epidemiology	PA is common but underdiagnosed – think about it with every hypertensive patient	21	1.75	1		
2	Increased morbidity	Untreated PA is associated with increased cardiovascular, renal, and metabolic risk when compared to blood pressure-matched essential hypertension	40	3.33	2.5		
3	Early screening	It is important to test for PA following a diagnosis of hypertension, by measuring aldosterone and renin	45	3.75	3		
4	Screening methods	The ARR is the key screening blood test for PA; however, it is important to recognize that results may be inaccurate due to interfering medications	55	4.58	4.5		
5	Pathophysiology	Pathophysiology: PA is an adrenal disease characterized by inappropriately high and autonomous aldosterone production and suppressed renin	58	4.83	5		
6	Treatment	PA has targeted treatment or potential cure	62	5.17	5		
7	Hypokalemia presence	Hypokalemia is not always present in PA	74	6.17	6.5		
8	Spectrum of condition	Spectrum of condition: PA can range in severity	81	6.75	7.5		
9	Screening guidelines	There are screening guidelines for PA as set out by the Endocrine Society	104	8.67	9		
ARR aldosterone renin ratio. PA primary aldosteronism							

highlights the importance of PA screening as an important teaching point for medical students.

Key knowledge area 2: Untreated PA is associated with increased cardiovascular, renal and metabolic risk when compared to BPmatched essential hypertension

Increased risk of poor cardiovascular, renal, and metabolic outcomes in inadequately treated PA is well documented in the literature. A retrospective French study comparing 459 patients with PA and 1290 with essential matched hypertension (EH) showed up to $3\times$ increased risk of myocardial infarction, atrial fibrillation, coronary artery disease, and heart failure.³⁰ A systematic review and meta-analysis of 3838 patients with PA compared to 9284 patients with EH also demonstrated an increased risk of stroke OR 2.58 (CI 1.93–3.45), atrial fibrillation OR 3.52 (CI 2.06-5.99), coronary artery disease OR 1.77 (CI 1.1-2.83) and heart failure OR 2.05 (CI 1.11-3.78) in the PA group.¹¹ Patients with PA also demonstrated accelerated renal damage compared to patients with EH evidenced by increased urinary albumin excretion, secondary to endothelial dysfunction caused by excess aldosterone.^{31,32} Specifically, preclinical models have characterized the impact of aldosterone infusion on promoting renal inflammation and fibrosis via actions on the podocytes, infiltrating macrophages and stromal cells.³³ In humans, the Chronic Renal Insufficiency Cohort (CRIC) study identified median baseline serum aldosterone concentration to be higher among 3680 participants who developed chronic kidney disease, at 10.6 ng/dL compared to 9.6 ng/dL. When expressed as a continuous variable, there was an 11% higher risk for chronic kidney disease progression per doubling of serum aldosterone.34 The FIDELIO

study contributed further weight to the impact of aldosterone excess on renal dysfunction by demonstrating a lower risk of chronic kidney disease progression in a randomized clinical trial of mineralocorticoid receptor antagonist, finerenone.³⁵

Key knowledge area 3: It is important to screen for PA following a diagnosis of hypertension by measuring aldosterone and renin

The high prevalence of PA together with the universal issue of underdiagnosis, logically leads to the third highest-ranked knowledge area. Currently, the Endocrine Society guidelines outline a range of criteria for PA testing (as described above),²⁵ however, the expert panel established consensus that all patients should be screened upon their diagnosis of hypertension. Screening for PA in all adults with hypertension has recently been recommended by the European Society of Cardiology 2024 Hypertension Guidelines.³⁶

The benefit of routine screening is evident in the 5–15-fold increase in PA diagnosis following the implementation of the aldosterone to renin ratio (ARR) as a routine test for PA across five international centers.³⁷ Routine measurement of the ARR in treatment-naïve hypertensive patients in primary care led to the diagnosis of PA in 14%.²¹ Early screening of PA also avoids the confounding effect of most antihypertensive agents which commonly cause false negative ARR results.²⁵ Furthermore, early PA screening has been found to be cost-effective in health economic evaluation studies from China and Australia.^{38,39}

Practical implications

Evaluation of these top three consensus points demonstrated that expert consensus, while obtained via questionnaires, has a strong evidence base. Given that maintaining currency in medical education is usually achieved by virtue of the teachers and educational resources being up to date,⁴⁰ consensus on teaching points by international experts, including patient advocates, may be a valuable and time-efficient strategy to achieve currency.

This is particularly the case for PA as current popular medical textbooks and online information resources often contain gaps and outdated

information. In a review of original articles published in the New England Journal of Medicine between 2001 and 2010, 146 medical reversals were identified where emerging evidence led to a change in previously established practices.⁴¹ Further research analyzing popular online resources, including UpToDate and Best Practice, found between 23% and 60% variation between these resources and recently published articles on the same topics.42 While no formal research has been published about the currency of PA medical resources, given the current challenges facing screening and diagnosis, it can be inferred that a proportion of the existing literature fails to adequately articulate the prevalence of PA, the importance of screening and the ease of medical management with mineralocorticoid receptor antagonist such as spironolactone.25

With the rapid pace of medical innovation and changes in guidelines, clear teaching points as identified in this Delphi study can be incorporated into the medical curriculum to guide student teaching and assessment. Furthermore, to ensure that the key learning points are widely disseminated beyond individual medical schools, collaborations can be sought with popular learning resources.

Further research to evaluate the clinical impact of expert-consensus-guided PA teaching will be important for understanding how this strategy improves the diagnosis, management, and health outcomes of patients with PA.

Strengths and limitations

A key strength of this research is the inclusion of both expert clinicians/educators and patients with lived experience of PA. The engagement of patients brings valuable insights into the practical and patient-centered aspects of care. An extensive literature search did not identify any other studies that utilized the Delphi process to establish learning points for students. This unique approach to developing education content has enabled us to identify and prioritize critical knowledge areas for PA that are important to both clinicians and consumers, creating a focused and relevant framework for curriculum development.

While the expert panel is geographically diverse, it consisted of a relatively small number of experts

with 13 in total, including only two consumers. This may have limited the breadth of perspectives, although the selected experts are highly experienced in the PA field and the consumers are affiliated with patient advocacy groups that represent thousands of voices.

Another limitation to the key knowledge areas identified by expert consensus is that they can become outdated over time. However, the three key areas identified in our study are unlikely to change in the near future, especially as the recent European Society of Cardiology Guidelines for the management of hypertension has just recommended that PA screening be considered in all adults with hypertension.⁴¹

Finally, it is important to note that our study has focused on what medical students should learn rather than what their knowledge gaps are and how the gaps can be filled. The next stage of research is to apply the key knowledge areas to student assessments and evaluate the coverage of these areas in popular learning resources.

Conclusion

Clinicians and patients with experience in PA reached consensus on nine key knowledge areas about PA through a modified Delphi process with the top three focusing on the underappreciated prevalence of PA, the high cardiovascular, metabolic, and renal risk associated with PA, and the importance of screening. These results provide a useful tool for evaluating the adequacy of current teaching about PA in medical schools and assessing the students' knowledge of PA.

The dynamic nature of medical advancements poses significant challenges in ensuring that healthcare providers are equipped with the most current and accurate knowledge. The prevalence of outdated information in widely used medical resources and the observed gaps in educational content underscore the need for continuous updates to medical curricula. Despite evidence showing that targeted education improves patient outcomes, variability in curriculum development and a lack of standardization contribute to inconsistent training across medical schools. Addressing these issues through expert consensus and curriculum reform is essential to enhance the accuracy of medical education and improve patient care, particularly in areas like PA where underdiagnosis remains a concern. Once these students transition to practicing clinicians it is hoped the knowledge will translate to improved diagnosis of PA thus reducing the burden of PA-associated morbidity in patients with hypertension.

Declarations

Ethics approval and consent to participate

All Delphi panel participants consented to involvement in this study and dissemination of its findings. All methods were carried out in accordance with the WMA Declaration of Helsinki -Principles for Medical Research Involving Human Subjects. The study was approved by the Monash University Human Research Ethics Committee as a clinical audit/Quality Assurance and Evaluation Activity (HREC Reference Number: QA/74597/MonH-2021-264596). As this study does not involve patient information or intervention, there are minimal risks to consider. Informed consent to participate was obtained from all participants in the study. Written consent was obtained from all panel participants (clinicians and consumers) for their involvement and contributions to this Delphi study.

Consent for publication Not applicable.

Author contributions

Jocelyn Widjaja: Data curation; Formal analysis; Investigation; Project administration; Writing – original draft.

Jun Yang: Conceptualization; Data curation; Resources; Supervision; Writing – review & editing.

Julia Harrison: Conceptualization; Formal analysis; Supervision; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

All the information required for the reproduction of the results can be obtained from author Jocelyn Widjaja upon reasonable request.

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