Review Article

Feasibility of focused parathyroidectomy in developing countries—a scoping review

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Background: The mainstay of treatment of primary hyperparathyroidism involves a parathyroidectomy, which depending on the number of affected parathyroid glands and the availability of resources, may involve a bilateral neck exploration with four gland assessment or a minimally invasive, focused parathyroidectomy (FP) necessitating pre-operative localisation. The feasibility of the latter is yet to be demonstrated in developing countries.

Methods: A scoping review was performed with published literature evaluated from the past 15 years (2007 & onwards). Articles were screened and only included if they discussed FP, preoperative localisation, economic impact and they originated from a developing country (upper middle or lower middle-income).

Results: A total of 18 articles met the inclusion criteria, comprising seven developing countries (two upper middle-income and five lower middle-income countries). Preoperative localisation was performed in all studies, with overall accuracy rates of 75.5% for ultrasound and 85.7% for ^{99m}Tc sestamibi. A total 1,202 patients (70%) had FP. Five hundred and fifty-five patients underwent FP without intraoperative adjuncts and 647 underwent FP with intraoperative adjuncts, with adjusted cure rates of 95.3% and 99.2% respectively. Overall cure rate for FP was 96.4%.

Conclusions: With access to accurate preoperative localisation and excellent cure rates with and without intraoperative adjuncts, we conclude that FP is feasible in developing countries.

Keywords: Primary hyperparathyroidism; parathyroidectomy; developing countries; focused parathyroidectomy (FP); low-income

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Introduction

The 'gold standard' operative treatment of primary hyperparathyroidism (HPT) has been bilateral neck exploration (BNE) since the first parathyroidectomy in 1925, with excellent cure rates of greater than 95% demonstrated (1). Cure is defined as re-establishing sustained normocalcaemia that persists for at least 6 months post surgery (2,3). The rationale for BNE at the time was the knowledge of multi-gland disease coupled with the inability to identify specific diseased glands preoperatively. van Heerden *et al.* [1991] demonstrated a cure rate of 99.5% in 379 patients with primary HPT undergoing BNE (4). Consistently high success rates were further

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demonstrated, revealing this procedure to be reliable and easily reproducible (5,6).

Focused parathyroidectomy (FP) was conceived due to the realisation that in 80% of cases of primary HPT the aetiology is a single gland adenoma, allowing a more targeted approach to parathyroidectomy (7). However, FP is naturally entirely reliant on adequate preoperative localisation. The greatest advancement being the ^{99m}Technetium sestamibi, as described by Coakley *et al.* [1989] (8). Today, there are numerous preoperative localisation studies available viz; different types of sestamibi radionucleotide scans, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans and ultrasound (US), each with varying degrees of sensitivities.

Initially, certain authors were against the notion of FP, with some advising against the technique as they simply considered it to be a passing trend and misguided (9). They identified two main concerns with this technique. The first was that of inferior cure rates, highlighted by Delbridge *et al.* [2000] who assessed FP in 50 patients and demonstrated an inferior 84% cure rate with FP, significantly lower compared to the standard of care BNE's established 95% cure rate (10). These inferior cure rates were mostly due to "double adenomas" which can account for up to 10% of all parathyroid adenomas (11). However, since then, intraoperative adjuncts used during FP evolved significantly, with use of intraoperative nuclear scanning and rapid intraoperative parathyroid hormone (IOPTH) test, FP cure rates equalled that of BNE (12,13). When coupled with intraoperative assays, it also obviates the need of inspection of the remaining parathyroid glands (PGs) thus preventing the complications associated with BNE (14,15).

The second concern with FP was the cost, with some authors demonstrating a higher cost associated with FP compared to BNE, resulting from the requisite preoperative localisation tests and the addition of intraoperative adjuncts (16,17). However, since then, the cost of preoperative localisation studies decreased, and the literature reflected this by subsequently revealing FP to be cost effective comparative to BNE alone, balanced by the added cost of increased operative time and longer hospitalisation associated with the latter (18).

Subsequently, FP has been shown to be superior to BNE. Udelsman *et al.* in 2000 with 100 cases, in 2002 with 255 cases and in 2011 with 1,037 cases of FP demonstrated a higher cure rate with FP (99.4% *vs.* 97.1% with BNE) with reduced cost, morbidity and length of hospital stay (19-21). Numerous other authors have demonstrated consistent findings (22-24). The benefits of FP over traditional BNE include equivalent rates of cure (95–98%), with added benefits of: the ability to be performed under a local anaesthetic, outpatient recovery, shorter operative time, desirable cosmesis, reduced nerve injuries and elimination of permanent hypoparathyroidism (25,26). Thus, in the setting of positive preoperative localisation, FP has become the new standard of care.

Importantly however, the mounds of literature we are guided by emanate from the developed, 'high-income world', where resources are far more abundant, with remarkable strides made in healthcare resource allocation. Unfortunately, in a developing (middle-income) setting, with marked disparity between the private and public healthcare sector, resources are drastically limited, often to the point of tailoring guideline recommendations to local resource availability (27).

Therefore, despite the described cost-effectiveness of FP with requisite localisation and IOPTH in studies from developed world literature, a developing country may not be able to rationalise this cost. In addition to the cost, availability is a concern, which, when considered, would drastically affect the feasibility of this procedure over a

Highlight box

Key findings

- Focused parathyroidectomy is safe and feasible in developing countries.

What is known and what is new?

- Literature from high-income countries have shown focused parathyroidectomy to be superior in terms of cost, despite the prerequisite of localisation studies required in order for this technique to be performed. Literature has emerged from individual developing countries reporting their experience with this technique.
- This manuscript collates and analyses those articles from developing countries to assess if reported rates of localisation accuracy and cure associated with focused parathyroidectomy is in keeping with that of high-income countries.

What is the implication, and what should change now?

- By demonstrating the feasibility of this technique in certain developing countries, other developing middle-income countries, who have possibly considered this technique to be non-applicable, are now encouraged to embrace focused parathyroidectomy as the reported new gold standard, for well localised, single-gland disease primary hyperparathyroidism.

traditional BNE that requires no additional localization or intra-operative adjuncts.

This scoping review serves to ascertain the feasibility of FP in developing countries, considering the perceived additional cost and unclear availability of mandatory preoperative localisation studies along with requisite intraoperative adjuncts and the necessary skill and experience needed to facilitate this procedure successfully. We present this article in accordance with the PRISMA-ScR reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-57/rc).

Methods

This scoping review evaluated primary, secondary and tertiary literature, drawing from both published peer-reviewed and grey literature. The framework guide by Arksey & O'Malley [2005], including modifications published by Levac *et al.* [2010], were followed (28,29). The stages traversed include: (I) identifying the research question; (II) identifying the relevant studies; (III) study selection, with specified inclusion and exclusion criteria; (IV) charting the data and lastly; (V) collating, summarising and reporting the results. Primarily, the PRISMA-Scr extension framework and checklist was adhered to, with reporting of eligible studies via the PRISMA flow diagram. The eligibility of the research question was explored via the PCC framework (30).

To assess the eligibility of the research question, the PCC framework—namely: 'population, concept and context' framework, as recommended by the Joanna Briggs Institute (JBI), was employed (31). The population was identified as primary hyperparathyroid patients warranting parathyroidectomy. The concept was identified as cost and availability accounting for feasibility of FP comparative to BNE in developing countries. Finally, context was identified as developing countries.

An extensive literature search was conducted, using Boolean logic operators such as 'AND' & 'OR', with the following key terms: 'primary hyperparathyroidism', 'parathyroidectomy', 'surgery', 'ultrasound', 'nuclear medicine', 'developing countries', and 'cost'. The keywords used complied with Medical Subject Headings (MeSH) terms, adjoined with relevant subheadings & qualifiers, falling within the jurisdictions of the MeSH tree structures. To broaden the exposure to relevant articles, the following non-MeSH conforming keywords were additionally employed: 'focused parathyroidectomy', 'feasibility', 'low-income', 'economic viability', 'sestamibi' and 'intra-operative PTH'.

The search utilised the following library databases: PubMed/MEDLINE, Google Scholar, World Cat, Academic Search Complete via EBSCO host, Open Dissertations via EBSCO host, SA ePublications via SABINET African journals, SACat via OCLC and ProQuest. These prodigious evidence sources were identified through their phenomenal reputations as leaders in library database provision, enabling access to a large cohort of invaluable research papers.

All articles encountered were entered into an excel spreadsheet, structured under the heading of each source. Articles were further categorised according to search terms employed.

Articles were retrieved upon exploration of the literature via the aforementioned library databases. Screening was initiated firstly by means of confirming relevance based on review of each title of the studies retrieved. Thereafter, abstracts were scanned, followed by introductions and statements of purpose. If the studies fulfilled the purpose of this review, the countries of origin were then scrutinized and cross checked with the United Nations Development Program (UNDP) & World Bank (WB) list of developing/middle income countries to ensure the articles to be perused were relevant (32,33). Finally, the full texts were engaged.

The basis for which these studies were selected includes: (I) studies providing evidence on surgical management of primary hyperthyroidism, specifically discussing focused or minimally invasive parathyroidectomy; (II) studies providing evidence on preoperative localisation; (III) studies providing evidence on a developing world approach to parathyroidectomy; and (IV) studies providing evidence on economic burden of either parathyroidectomy option. The period explored was literature from the past 15 years (from 2007 onward). No restriction on language was employed, allowing for greater acquaintance.

Studies not meeting the inclusion criteria of: providing evidence on surgical management of primary hyperthyroidism; with specific discussion on focused/minimally invasive parathyroidectomy; providing evidence on preoperative localization; providing evidence on a developing world approach to parathyroidectomy and providing evidence on economic burden of either parathyroidectomy option were all excluded, including all studies published prior to 2007. Additionally, all studies exclusively describing endoscopic or minimally invasive video assisted FP were excluded.

Table 1 Evidence sources

Database	No. of studies encountered
PubMed	446
Google Scholar	217
ProQuest	132
Science Direct	61
WorldCat	39
Academic Search Complete	32
Sabinet	7
Langenbeck's Archive of Surgery	6
Total	940

The studies included for this review primarily comprises non-randomized evidence in the form of case series, cohort studies and 1 case report. Consequently, a trio of 'JBI critical appraisal tools' were employed to assess the quality of evidence, namely the 'case series checklist', 'cohort study checklist' and 'case report checklist' tools. These tools were completed by two reviewers independently, as recommended by the JBI. The Oxford Centre for Evidence-based Medicine (CEBM) grading was utilized to assess the level of evidence of the included studies. See Appendix 1 for 'JBI Critical Appraisal Tools'.

Results

A total of 940 relevant articles were encountered upon exploration of the literature from 8 different databases (see *Table 1*). After duplicates were removed and elimination by screening of article titles, abstracts, full texts and countries of origin, a total of 18 remaining articles fulfilled the purpose of this review and thus were included for study (see *Figure 1*).

In the 18 articles, a total 1,716 patients underwent parathyroidectomy from seven developing countries [five studies from South Africa (upper middle-income); five studies from India (lower middle-income); three studies from Pakistan (lower middle-income); two studies from Turkey (upper middle-income); one study from Egypt (lower middle-income); one study from Algeria (lower middle-income) and one study from Nigeria (lower middle-income)] (see *Table 2*).

FP was performed in 1,202 patients (70%) with 7 studies (38.9%) reporting on 647 patients having had FP with intraoperative adjuncts (including IOPTH, methylene blue, frozen section or the gamma probe) and 11 studies (61.1%) reporting on 555 patients having had FP without intra-operative adjuncts.

Cure rates from the studies included in this review for FP were reported in 15 (7 with intraoperative adjuncts & 8 without intraoperative adjuncts) of the 18 studies. Of the 15 studies with reported cure rates, only 11 (73%) met the definition of cure following parathyroidectomy, with a minimum of a 6-month follow-up. Consequently, only cure rates from these 11 studies were included in the statistical analysis. Cure rates ranged from 83.3% to 100%, with an overall cure rate of 96.4% (see *Tables 3*,*4*).

Preoperative localisation in these developing countries were performed by US and ^{99m}Tc sestamibi, with 1 study describing the use of ^{11}C methionine PET/CT as an additional localisation modality. Accuracy rates of localisation studies in these developing countries ranged from; 44–94% with US, 66.5–100% with ^{99m}Tc sestamibi and 71.4% for the ^{11}C methionine PET/CT (see *Table 5*).

Discussion

Whilst the operative management of primary HPT has undergone profound evolutionary changes resulting in FP being considered the new standard of care for cases of primary HPT with unequivocally localised single gland disease, as recommended by the American Association of Endocrine Surgeons (AAES) and the Fifth International Workshop on Primary Hyperparathyroidism, the concern for practitioners in developing low and middle-income countries is the relevance of the evolutionary changes and the applicability of its outcome, namely FP, considering the basis for it all emanates from developed high-income countries (53,54).

As demonstrated by Hurst *et al.* [2005] and Adhikari *et al.* [2021], evidence-based medicine and the guidelines they produce from high-income countries most often cannot be adhered to in resource constrained low and middle-income countries (55,56). As such, this review was conducted to address the question of feasibility of FP in terms of accessibility to and accuracy of preoperative localisation and adequacy of cure rates with this technique, in developing countries.

The first prerequisite to enable performing FP is adequate preoperative localisation. From this review, it was revealed that preoperative localisation was available in all developing countries from the articles included in this

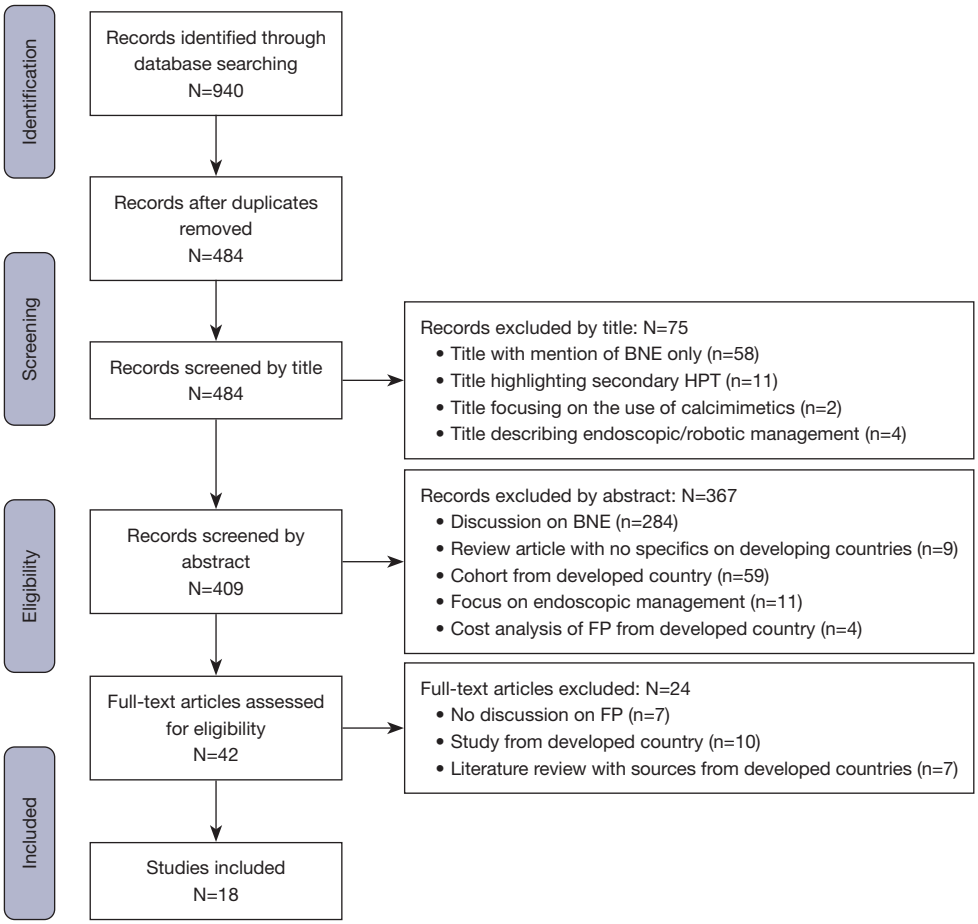

Figure 1 PRISMA flow chart of included studies (30). BNE, bilateral neck exploration; HPT, hyperparathyroidism; FP, focused parathyroidectomy.

review, with the most common modality used being the ^{99m}Tc sestamibi (used in all studies) followed by US (used in 16 of the 18 studies). The overall accuracy of ^{99m}Tc sestamibi and US for preoperative localisation in these developing countries were 85.7% and 75.7% respectively. The overall accuracy of combined US and ^{99m}Tc sestamibi was 95.2%. These results are in keeping with preoperative localisation rates reported from high-income countries.

Cheung *et al.* [2012] in their meta-analysis revealed sensitivities for ^{99m}Tc sestamibi and US of 78.9% and 76.1% respectively (57). Combined ^{99m}Tc sestamibi/US use for preoperative localisation has been reported to have a sensitivity of 96%, in keeping with the sensitivity of preoperative localisation from the developing countries in this study (58). In a single lower middle-income country, Nigeria, Olatoke *et al.* [2013] demonstrated preoperative localisation to be possible, but not feasible, as each ^{99m}Tc sestamibi test required a 250 km journey to access a facility with the necessary equipment (45).

Intraoperative adjuncts were used in 7 of the total 18 studies: IOPTH was used in three studies; frozen section in two studies; methylene blue in one study and the gamma probe in one study. Cure rates of the study were adjusted according to whether the correct definition of cure was achieved in a study, with statistical exclusion of the study if the standard definition was not met (see *Table 6*). The adjusted cure rate for patients undergoing FP with IOPTH was 98.5%, with an overall cure of 99.2% for patients undergoing FP with intraoperative adjuncts. In the remaining studies of FP without intraoperative adjuncts, the overall cure rate was 95.3%. These figures from the developing countries included are in keeping with reported cure rates from high-income countries as demonstrated by Quinn *et al.* [2021]. In their meta-analysis the authors

Table 2 Characteristics of studies

Study number	Study	Title	Year	Country & UNDP/WB classification (34)	Study type & level of evidence	No. of patients	Main outcomes
1.	Usta *et al.* (35)	A 20-Year Study on 190 Patients With Primary Hyperparathyroidism in a Developing Country: Turkey Experience	2015	Turkey (developing/ upper-middle income country)	Cohort study level 2b	190	Preoperative localisation accuracy rate by US & ^{99m}TcS was 82.6%, and 89.4% respectively. Combined ^{99m}TcS & US yielded a 92% localisation accuracy rate. FP with intraoperative frozen section analysis only was performed in 167 patients and resulted in good cure rate of 99.52%—similar cure rate to BNE, with significantly decreased operative time, hospital stay & hospital cost
2.	Siddiqui *et al.* (36)	Changing paradigms in the surgical management of hyperparathyroidism at a tertiary care hospital in a developing country	2019	Pakistan (developing/ lower-middle income country)	Cohort study level 2b	72	Preoperative localisation accuracy rate by US & ^{99m}TcS was 71.1%, and 90.1% respectively. FP without intraoperative adjuncts, was performed in 27 of the total 72 cases with a cure rate of 92.6%, similar cure rate of BNE (90.5%) with fewer complications—demonstrating this technique to be both effective & reasonable
3.	Paruk *et al.* (37)	Characteristics, management and outcome of primary hyperparathyroidism in South Africa: a single-centre experience	2013	South Africa (developing/upper-middle income country)	Case Series level 4	28	Preoperative localisation was only performed with ^{99m}TcS, with an accuracy rate of 93.7%. FP without IOPTH monitoring was performed in 19 of 28 patients, with a cure rate of 94.7%. Demonstrating the safety & feasibility of this technique
4.	Mallikarjuna *et al.* (38)	Five-year Retrospective Study on Primary Hyperparathyroidism in South India: Emerging Roles of Minimally Invasive Parathyroidectomy and Preoperative Localization with Methionine Positron Emission Tomography-Computed Tomography Scan	2018	India (developing/lower-middle income country)	Case Series level 4	54	Preoperative localisation accuracy rate by US & ^{99m}TcS was 72.2%, and 70.6% respectively. Additionally, C11 methionine PET was used for localisation in a portion of patients, with an accuracy rate of 71.4%. 43 patients underwent FP without intraoperative adjuncts, more than three-quarters (79.6%) of the total patients during the 5-year period, demonstrating this technique to be feasible in this locality of South India. No cure rate was reported
5.	El-Hady *et al.* (39)	Focused parathyroidectomy for single parathyroid adenoma: a clinical account of 20 patients	2018	Egypt (developing/ lower-middle income country)	Case Series level 4	20	Preoperative localisation accuracy rate by US & ^{99m}TcS was 75%, and 90% respectively. Combined ^{99m}TcS & US yielded a localisation accuracy rate of 95% in this setting. FP without IOPTH monitoring was performed in 19 of 20 patients, with a cure rate of 95% & no major complications reported, with the authors concluding this technique to be safe and feasibility, even without intra-operative adjuncts
6.	Sen *et al.* (40)	Focused Parathyroidectomy Under Local Anesthesia – A Feasibility Study	2019	India (developing/lower-middle income country)	Case Series level 4	65	Preoperative localisation was performed by US & ^{99m}TcS, however the accuracy rate was not determined in this study as only patients with 100% concordance with pre-operative localisation were included in this study. FP without IOPTH monitoring was performed in 48 of 65 patients. 30 of the 48 cases were performed under local anaesthetic, with significantly reduced cost demonstrated and a cure rate of 100% reported, concluding this procedure to be safe and feasible
7.	Rawat *et al.* (41)	Minimally Invasive Parathyroidectomy as the Surgical Management of Single Parathyroid Adenomas: A Tertiary Care Experience	2023	India (developing/lower-middle income country)	Case Series level 4	116	Preoperative localisation accuracy rate by US & ^{99m}TcS was 93.10%, and 96.55% respectively. Combined ^{99m}TcS & US yielded a localisation accuracy rate of 100% in this study. FP with IOPTH monitoring was performed in all patients with a cure rate of 99.13% reported, with the authors concluding this procedure to be safe and feasible
8.	Nouikes Zitouni (42)	Monocentric experience of primary hyperparathyroidism surgery in Algeria	2021	Algeria (developing/ lower-middle income country)	Cohort study level 2b	62	Preoperative localisation accuracy rate by US & ^{99m}TcS was 60.7%, and 66.5% respectively. Combined ^{99m}TcS & US accuracy rate was 100% in this study. 28 of 62 patients had MIP (unilateral exploration + focused) without IOPTH monitoring, 18 of whom specifically had a FP, with a cure rate of 83.3%—demonstrating the safety & feasibility of this procedure
9.	Van Wyngaard (43)	Pre operative localisation and surgical outcomes for Primary Hyperparathyroidism (PHPT): an 11 year review at a South African hospital	2018	South Africa (developing/upper-middle income country)	Case Series level 4	98	Preoperative localisation accuracy rate by US & ^{99m}TcS was 44%, and 75% respectively. FP with IOPTH monitoring was performed in 76% of patients [75 patients] with the remaining 24% having had BNE. The overall cure rate was 94%. This study demonstrates the safety and feasibility of FP
10.	MacRobert *et al.* (44)	Single gland versus multigland disease in primary hyperparathyroidism at the Wits Donald Gordon Medical Centre in Johannesburg, South Africa	2021	South Africa (developing/upper-middle income country)	Cohort study level 2b	252	Preoperative localisation accuracy rate by US & ^{99m}TcS for single gland disease was 77.1%, and 72.9% respectively. Combined ^{99m}TcS & US yielded a sensitivity of 79.7% for single gland disease. FP was performed in 44.8% of patients [113 patients] with no documented use of intraoperative adjuncts, with the remaining 139 patients having had BNE. A 92% reduction in hypercalcaemia was demonstrated, however no cure rate was reported due to lack of 6-month postoperative results. This study re-enforced the notion that BNE is the gold standard, however, with a predominance of single gland disease (83.3%), this study advocates equally for FP and BNE
11.	Olatoke *et al.* (45)	Serial pathologic fractures of five long bones on four separate occasions in a patient with primary hyperparathyroidism, challenges of management in a developing country: a case report	2013	Nigeria (developing/ lower-middle income country)	Case Report	1	In this case report, the parathyroid adenoma was successfully localised with combined US and ^{99m}TcS. Despite numerous challenges such as the ^{99m}TcS facility being 250 km away and PTH testing needing to be done in another African country, the Authors persisted and were able to perform a focused unilateral exploration, with a demonstrated drop in postoperative PTH levels. This case report demonstrates while it may be possible to perform a parathyroidectomy in this country, with PTH needing to be performed in another country and the distance of travel required for pre-operative localisation, there are significant challenges associated with both BNE & FP
12.	Bombil *et al.* (46)	Sonar guided focused parathyroidectomy under cervical block	2018	South Africa (developing/upper-middle income country)	Case Series level 4	15	This study looked specifically at FP performed under a cervical block +/- local anaesthetic. Although no exact rate was provided, combined US and ^{99m}TcS was used for preoperative localisation, with a report of good localisation/concordance, and mention of only one discordant finding. 100% of patients had a FP with complete resolution of hypercalcaemia in all patients, demonstrating this surgical technique to be safe and feasible

Table 2 (*continued*)

Table 2 (*continued*)

Study number	Study	Title	Year	Country & UNDP/WB classification (34)	Study type & level of evidence	No. of patients	Main outcomes
13.	Yadav *et al.* (47)	Surgical Management of Primary Hyperparathyroidism in the Era of Focused Parathyroidectomy. A Study in Tertiary Referral Centre of North India	2019	India (developing/lower-middle income country)	Cohort study level 2b	373	Preoperative localisation accuracy rate by US & ^{99m}TcS was 80%, and 86% respectively. FP was performed in 49.32% of patients [184 patients], with IOPTH monitoring being performed in 85% of FP cases [151patients] and 66.21% of total cases [247]. There was no statistical difference in cure with (98.02%) or without IOPTH (100%). An overall cure rate of 97.8% was reported, with a cure rate of 98.92% for FP, statistically similar to that of BNE, with the authors concluding FP to be safe and feasible, with or without IOPTH monitoring
14.	Dahiya *et al.* (48)	Surgical outcome after focused parathyroidectomy: experience from a tertiary care centre in North India	2021	India (developing/lower-middle income country)	Case Series level 4	192	Preoperative localisation accuracy rate by US & ^{99m}TcS was 83%, and 88% respectively. FP without IOPTH was performed in all 192 patients, with a cure rate of 97.92%. The authors conclude the technique to be the treatment of choice for sporadic primary HPT, when there is accurate pre-operative localisation, thus demonstrating the safety and feasibility of this technique
15.	Alikor *et al.* (49)	The Usefulness of ^{99m}technetium-sestamibi Parathyroid Scintigraphy in Preoperative Localization of Parathyroid Adenoma in Patients with Primary Hyperparathyroidism at an Academic Hospital in South Africa	2017	South Africa (developing/upper-middle income country)	Case Series level 4	11	Preoperative localisation was performed only with ^{99m}TcS, which demonstrated a sensitivity of 100% in this study, allowing FP in all 11 patients, with intraoperative use of the gamma probe (radio-guided). Cure rate was reported to be 100%, with 14 adenomas removed from the total 11 patients (2 with multiple adenomas detected at pre-operative localisation and confirmed intra-operatively). The authors conclude ^{99m}TcS to be useful in this setting and have resultantly shown FP to be feasible
16.	Afzal *et al.* (50)	Management of hyperparathyroidism: a five year surgical experience	2011	Pakistan (developing/lower-middle income country)	Case Series level 4	35	32 of the total patients had primary HPT, with preoperative localisation with combined ^{99m}TcS & US, yielding a reported 100% accuracy rate. No individual localisation rates were provided. FP without IOPTH was performed in 27 cases (84.4%) and BNE in 5 cases (15.6%). 100% cure rate was revealed for both techniques, demonstrating safety and feasibility of this technique, with the authors concluding accurate pre-operative localisation & safe surgery allows total cure for these patients
17.	Baloch *et al.* (51)	Surgical management of hyperparathyroidism	2007	Pakistan (developing/lower-middle income country)	Case Series level 4	16	11 of the total 16 patients in this case series presented with primary HPT, with preoperative localisation rate by combined US and ^{99m}TcS accurate in 100% of cases, allowing FP, with intraoperative methylene blue, in this group. The remaining patients had secondary HPT with parathyroid hyperplasia requiring total parathyroidectomy via BNE. These techniques both demonstrated a 100% cure rate, with the authors concluding both techniques to be satisfactory treatments for their respective parathyroid pathology (primary *vs.* secondary)
18.	Koyuncu *et al.* (52)	Minimally invasive surgery in primary hyperparathyroidism	2023	Turkey (developing/upper-middle income country)	Case Series level 4	116	Preoperative localisation accuracy rate by US & ^{99m}TcS was 94%, and 95% respectively. FP with intraoperative frozen section was performed in all 116 patients, with a cure rate of 94.2% and morbidity of 1.7%. The authors conclude the technique to be the preferred treatment of choice for single gland disease, demonstrating the safety and feasibility of this technique

UNDP, United Nations Development Program; WB, World Bank; US, ultrasound; 99mTcS, 99mTc sestamibi; FP, focused parathyroidectomy; MIP, minimally invasive parathyroidectomy; BNE, bilateral neck exploration; IOPTH, intraoperative parathyroid hormone; PET, positron emission tomography; HPT, hyperparathyroidism.

Table 3 Statistical analysis study inclusions

Study number	Study	Cure rate	Follow-up	Cure correctly defined
1.	Usta *et al.* (35)	99.52%	8.4 years	Yes
2.	Siddiqui *et al.* (36)	92.6%	1 year	Yes
3.	Paruk *et al.* (37)	94.7%	2 years	Yes
5.	El-Hady *et al.* (39)	95%	6 months	Yes
6.	Sen *et al.* (40)	100%	6 months	Yes
7.	Rawat *et al.* (41)	99.13%	6 months	Yes
8.	Nouikes Zitouni (42)	83.3%	6 months	Yes
13.	Yadav *et al.* (47)	98.92%	6 months	Yes
14.	Dahiya *et al.* (48)	97.2%	6 months	Yes
16.	Afzal *et al.* (50)	100%	1 year	Yes
17.	Baloch *et al.* (51)	100%	6 months	Yes

Table 4 Cure rates

Operative procedure/adjunct	Number of studies	Number of patients (%)	Cure rate	Number of studies included in statistical analysis
Focused parathyroidectomy	18	1,202	96.4%	11*
Without intra-operative adjuncts	11	555 (46.2)	95.3%	8
Intra-operative adjuncts total	7	647 (53.8)	99.2%	4
IOPTH	3	342 (28.5)	98.5%	2
Frozen section	2	283 (23.5)	99.5%	1
Methylene blue	1	11 (0.9)	100%	1
Gamma probe	1	11 (0.9)	–	0

*, for the number of studies used in statistical analysis of cure rate, 1 study included a cohort describing both FP with intra-operative adjuncts and FP without, hence final column row 2 + row 3 ≠ row 1. IOPTH, intraoperative parathyroid hormone; FP, focused parathyroidectomy.

Table 5 Preoperative localisation

Modality	No. of studies performed in	No. of studies describing individual accuracy rates	Accuracy range	Overall accuracy
US	16/18 (88.9%)	11/18	44–94%	75.7%
^{99m}Tc sestamibi	18/18 (100%)	13/18	66.5–100%	85.7%
Combined US & ^{99m}Tc sestamibi	16/18	7/18	79.9–100%	95.2%
^{11}C methionine PET/CT	1	1	–	71.4%

US, ultrasound; ^{99m}Tc sestamibi, ^{99m}Technetium sestamibi; ^{11}C methionine PET/CT, ^{11}carbon methionine positron emission tomography/computed tomography.

Table 6 Studies excluded from statistical analysis

Study number	Study	Cure rate	Follow-up	Cure correctly defined
4.	Mallikarjuna *et al.* (38)	Not stated	Nil	No
9.	Van Wyngaard (43)	94%	Nil	No
10.	Macrobert *et al.* (44)	Not stated	Nil	No
11.	Olatoke *et al.* (45)	Not stated	15 months	No
12.	Bombil *et al.* (46)	100%	3 months	No
15.	Alikor *et al.* (49)	100%	Nil	No
18.	Koyuncu *et al.* (52)	94.2%	Nil	No

compared cure rates of patients undergoing FP with *vs.* without IOPTH. The authors reported cure rates of 98% for FP with IOPTH and 94.8% for FP without (59).

The lowest cure rate in this review was reported by Zitouni *et al.* [2021] from the lower middle-income Algeria, who reported a cure rate of 83.3% with FP (42). The limitation with this study was the low sample size of only 18 patients who underwent FP, thus the 83.3% represents 15 of the 18 cured, with 3 patients having had persistence. Additionally, individual preoperative localisation accuracy rates were relatively low in this study, with US accurate in 60.7% of cases and ^{99m}Tc sestamibi accurate in 66.5% of cases.

With the 18 studies from developing countries included in this review, a total of 1,202 patients underwent FP with an overall cure rate of 96.4%. This is in keeping with reported cure rates from high income countries. Ishii *et al.* [2018] in their meta-analysis of 5,282 patients, from 14 included studies having undergone FP, demonstrated an overall cure rate of 96.9% (60).

From this review, it is evident that not only is preoperative localisation accessible and accurate in these developing countries, but FP is also successfully being performed within these regions. The two lower middle-income countries with difficulties were Nigeria and Algeria, demonstrating that perhaps the upper-middle income developing regions are currently better suited to adapting to this minimally invasive technique.

Limitations

There were only seven developing countries included in this review, thus limiting the relevance of this review to other developing countries. A small number of studies did not report individual preoperative localisation rates or overall cure rates, thus distorting representation. The quality of evidence of studies included in this review mostly (17/18) comprise of case series and cohort studies, however one study, number 11 by Olatoke *et al.*, is a single case report, thus representing low quality evidence. Additionally, this study offered no statistical benefit, however this report of only a single case is due to and demonstrates the challenges of FP in this country, which speaks to the aim of this review (45,61).

Conclusions

Preoperative localisation is available in developing countries, with adequate accuracy rates, in keeping with rates described in literature from high-income countries. FP is performed in developing countries with adequate cure rates in keeping with that of randomised controlled trials (RCTs) published from high-income countries. Although some developing countries lack availability of certain intraoperative adjuncts, this was not prohibitive and cure rates with or without these adjuncts were similar in these countries. With the established availability and impressive accuracy rates of preoperative localisation and the demonstrated success rates of FP, it is evident this technique is safe and feasible in developing countries.

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