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ORIGINAL ARTICLE

Current trends in surgery for renal hyperparathyroidism (RHPT)—an international survey

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Abstract
Purpose The indications and results of preoperative localization, surgical strategy, indication for thymectomy, the application of intraoperative parathyroid hormone (PTH) monitoring, cryopreservation, and replantation of cryopreserved parathyroid tissue are not well documented in renal hyperparathyroidism (RHPT). The current trends in surgery for RHPT are to be evaluated in an international online survey.
Methods Thirty-three questions regarding preoperative localization, surgical management of RHPT, intraoperative PTH monitoring, immediate/delayed autotransplantation (AT), and parathyroid cryopreservation were sent to members of various societies of endocrine surgeons.
Results The data from 86 responses were analyzed, 61.6 % reported more than 50 parathyroid surgeries per year, and 62.7 % operated on less than 16 patients with RHPT per year. Subtotal or total parathyroidectomy (with/without AT) was the standard procedure in 98.8 % of the cases. Immediate AT was performed in 40.7 % (72.7 % in the forearm). In most patients, the onset of graft function was documented later than 1 week after AT. Cryopreservation was routinely performed in 27.4 %. In 10.7 %, replantation was performed in more than five patients (hypo- or aparathyroidism: $n=41$; fresh graft failure: $n=13$; reoperations: $n=9$). Intraoperative PTH monitoring (in RHPT) was routinely used in 46.2 %. Its influence on surgical strategy was confirmed in 40 %.
Conclusions The survey reflects the divergent strategies applied for AT, cryopreservation, and PTH monitoring in RHPT.

Keywords Renal hyperparathyroidism · Parathyroid hormone monitoring · Cryopreservation · International survey · Autotransplantation

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Introduction

Secondary (renal) hyperparathyroidism (RHPT) is a common disorder in patients with chronic kidney disease. It is caused by permanent stimulation of the orthotopic and heterotopic parathyroid tissue due to phosphate retention, (reactive) hypocalcemia, and vitamin D insufficiency [1]. According to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [2], the indication for surgery is "severe hyperparathyroidism" which cannot be managed with medical treatment and persists longer than 6 months. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines [3] define "severe hyperparathyroidism" in terms of "persistent serum levels of intact parathyroid hormone (PTH) >800 pg/mL (88.0 pmol/L), associated with hypercalcemia and/or hyperphosphatemia that are refractory to medical therapy." While clear surgical guidelines are missing, there is an ongoing discussion as to which surgical procedure is the "best standard." Furthermore, there are no standard recommendations regarding transcervical thymectomy, application of intraoperative PTH monitoring (IOPTH), or cryopreservation of parathyroid tissue and its replantation on demand. The aim of this study was to evaluate the current standard procedures and experiences of endocrine surgeons worldwide in RHPT in an online survey.

Materials and methods

A survey with 33 questions (see the "Appendix") was designed to assess experience with parathyroid surgery in general, surgical management of RHPT in particular, and IOPTH and cryopreservation of parathyroid tissue. LimeSurvey, an "open source" web application, was used. The questions are detailed in Table 1. An email invitation to participate (Fig. 1) was sent to all members of the International Association of Endocrine Surgeons (475 email invitations), the European Society of Endocrine Surgeons (202 email invitations), and the German Society of Endocrine Surgeons (Chirurgische Arbeitsgemeinschaft Endokrinologie, 305 email invitations). After registration on the webpage http://www.parathyroid-surgery.net, a link to an anonymous questionnaire was sent to the participant. Possible multiple memberships in more than one of the participating societies were not ruled out, but double registration was prevented by a technical shutoff. A response rate could therefore not be calculated. Institutional data were provided voluntarily. Optionally, the survey was printed out and submitted via fax or mail.

Results

Eighty-six analyzable responses from different institutions were returned (78 complete, eight incomplete; Fig. 1). Fifty-three responses (61.6 %) were sent back from institutions in Europe, 20 (23.3 %) from North America, seven (8.1 %) from Asia, and six (7 %) from Australia.

Frequency of surgery for RHPT

Fifty-three questionnaire participants (61.6 %) document more than 50 parathyroid surgeries per year. The majority (n=54, 62.8 %) operate on less than 16 RHPT patients annually (Fig. 2).

Localization studies

Regarding RHPT, ultrasound (n=31; 36 %) and sestamibi scintigraphy (n=8; 9.3 %) are the main localization studies. Eighteen participants (20.9 %) operate without preoperative localization whatsoever. In combination, ultrasound and sestamibi scintigraphy are used by 29 (33.7 %).

Surgical strategy

Subtotal or total parathyroidectomy—with or without immediate autotransplantation (AT)—are the standard procedures for 85 participants (98.8 %). One participant reported to excise only sestamibi-positive gland(s) only. Surgical procedures compared with the number of surgeries for RHPT per year are demonstrated in Table 2.

Thymectomy

Transcervical thymectomy is routinely performed by 64 questionnaire responders (74.4 %). With a positive localization, 22 (25.6 %) even perform transsternal exploration to remove an ectopic gland during the initial operation.

Immediate AT

Thirty-five participants (40.7 %) perform immediate AT routinely, and 31 (36 %) do not. Ten (11.6 %) perform AT depending on the results of IOPTH, eight (9.3 %) only do so in patients with a functioning kidney graft, and two (2.3 %) in those on hemo- or peritoneal dialysis. Implantation sites include the forearm (n=40; 72.7 %), sternocleidomastoid muscle (n=9; 16.4 %), or other locations (e.g., presternal region, infraclavicular region, lower extremities; n=6; 10.9 %).

Graft function

Most of the participants control graft function with PTH blood samples [39 (62.9 %) with serum PTH and 17 (27.4 %) in the grafted vs. non-grafted arm]. A temporary implantectomy ("Casanova test") is routinely performed by five (8.6 %). One participant (1.6 %) does not control parathyroid graft function. The onset of graft function is unknown or is not evaluated in 14 centers (23.3 %).

Table 1 Topics of the international survey (for further details, see the "Appendix")

Topic	Sections—details asked	No. of questions
Institutional data	Country, city/institution (optional), experience with parathyroid surgery	6
Surgery	Preoperative localization, surgical strategy	5
Immediate AT	Technique, replantation, function/results	6
Cryopreservation	Technique, storage time	3
Delayed AT (of cryopreserved tissue)	Indication, technique, function/results	8
IOPTH	Assay, technique, interpretation, influence on strategy	5

AT Autotransplantation, *IOPTH* intraoperative PTH monitoring

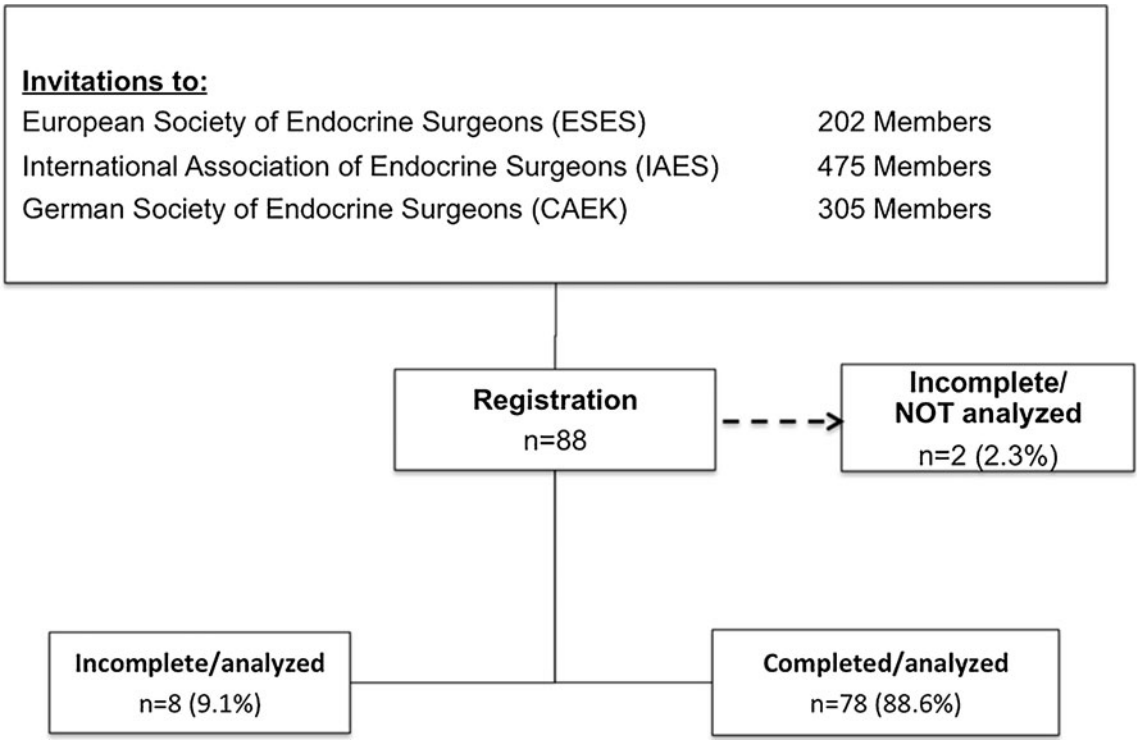

Fig. 1 Email invitation and response

Thirty-one of 46 participants (67.3 %) document graft function later than 1 week after immediate AT (Fig. 3).

Intraoperative PTH monitoring

Thirty-six participants (46.2 %) routinely use IOPTH, while 19 (24.4 %) only do so for scientific reasons or during reoperations. Moreover, an influence on surgical strategy was stated by 22 (40 %). For 21 responders (38.2 %), IOPTH guides further surgical exploration or AT. Time points for blood sampling and the interpretation of PTH curves vary (Table 3). Most participants use interpretation criteria similar to or adapted from primary hyperparathyroidism (PHPT) with a wide extent of variability.

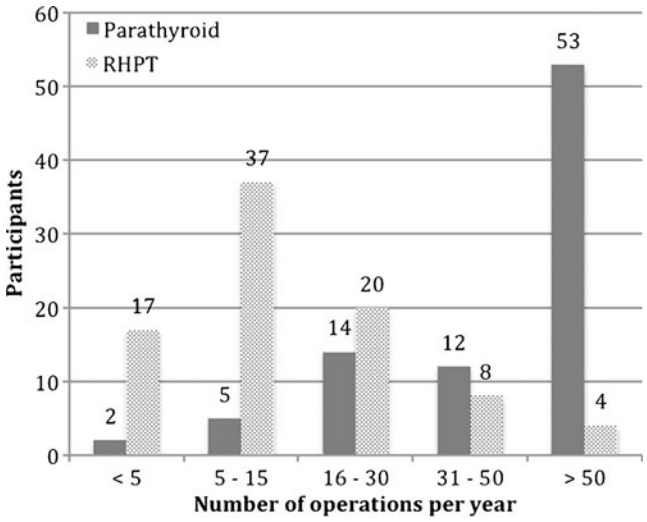

Fig. 2 Frequency of PTH surgery: primary HPT and secondary (renal) HPT. *Parathyroid* (*n*) procedures for primary hyperparathyroidism. *RHPT* (*n*) procedures for secondary (renal) hyperparathyroidism

Cryopreservation and delayed AT

Twenty-three centers (27.4 %) cryopreserve parathyroid tissue routinely during surgery for RHPT. Eleven centers (13.1 %) perform cryopreservation in selected patients, and 50 centers (59.5 %) do not apply this strategy. The storage time of cryopreserved tissue is shown in Table 4. Metachronous replantation is reported by 28 of 34 centers (82.4 %). However, 25 of 28 (89.3 %) performed replantation in five or less patients. The sites of replantation are the forearm (n=25, 89.3 %), sternocleidomastoid muscle (n=2, 7.1 %), or lower extremity (n=1, 3.6 %). Eleven of 28 participants (39.3 %) evaluate the graft before implantation (pathological examinations to determine the rate of necrosis; microbiological tests). The indications (multiple choices were possible) were hypo- or aparathyroidism in patients without immediate parathyroid autograft (n=41), fresh graft failure (n=13), and after reoperations (n=9). Basal PTH levels (n=23; 60.5 %) or blood samples comparing the PTH levels of the grafted vs. the non-grafted arm (n=9;

Table 2 Surgical procedures as compared with number of surgeries for RHPT per year

RHPT-surgeries (*n*) per year	MIBI pos(*n*)	SPTX (*n*)	Total PTX+AT (*n*)	Total PTX-AT (*n*)	Σ (*n*)
Less than 5	1	5	9	2	17
5–15	0	18	15	4	37
16–30	0	12	8	0	20
31–50	0	5	3	0	8
More than 50	0	2	2	0	4
Σ (*n*)	1	42	37	6	86

n number of centers/participants, *MIBI pos* excision of sestamibi-positive glands only, *SPTX* subtotal parathyroidectomy (3 ½ glands), *Total PTX +AT* total parathyroidectomy with autograft, *Total PTX-AT* total parathyroidectomy without autograft

23.7 %) are documented to control graft function post-operatively, respectively.

Additionally, the Casanova test or sestamibi scintigraphy are used by five (13.2 %) and one (2.6 %) responder, respectively. Onset of graft function is demonstrated between days 4 and 14 post-surgery in 22.6 %, it is seen before that time in 13.6 %, and later in 63.7 % (Fig. 3). Among the autografted patients, 40.3±30.9 % (mean±standard deviation) are reported to need no substitution, while 50.1± 32.1 % needed "mild" calcium and/or vitamin D substitution. About 9 % of the patients experienced disease recurrence in the autograft.

Discussion

The focus on RHPT treatment is mainly medical. Currently, cinacalcet is the only available oral calcimimetic [4] and therefore an important agent for "medical parathyroidectomy." It significantly influences PTH, calcium, and phosphorus metabolism and reduces the negative actions of secondary HPT: The fracture risk, the rate of hospitalization for cardiovascular disease, and the number of patients requiring parathyroid surgery are decreased [5, 6]. Indications for surgery are defined by the KDIGO [2] and NKF KDOQI guidelines [3]. However, patients may develop resistance to

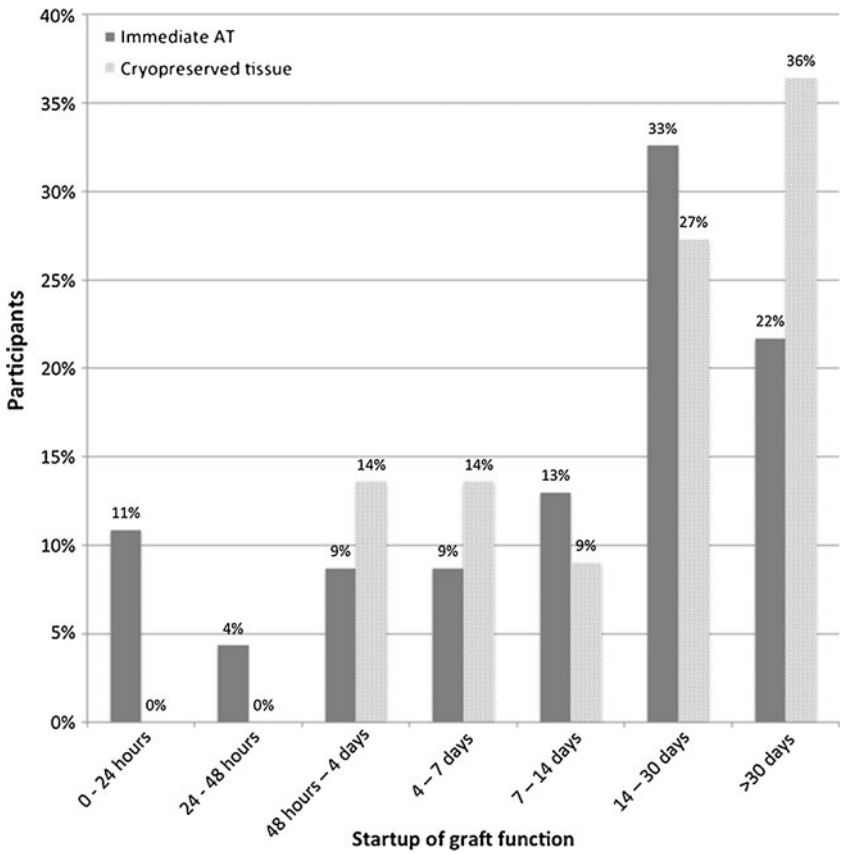

Fig. 3 Onset of graft function. *AT* autotransplantation

Table 3 Time points of blood sampling performing intraoperative PTH monitoring

Time point	Participants (*n*)
Before skin incision	50
Visualization of dominating gland ("adenoma")	6
Excision of the gland	11
5 min after excision	22
10 min after excision	36
15 min after excision	23
20 min after excision	19
25 min after excision	1
30 min after excision	10
Others	7

cinacalcet or after initially sufficient PTH suppression and show recurrently high PTH values. It has been recently demonstrated that—following ineffective "medical parathyroidectomy"—PTH, calcium, and phosphorus metabolism may significantly improve with "surgical parathyroidectomy." However, not all parameters post-surgery are then within the "target range" according to current nephrological guidelines [7]. There are no mandatory surgical guidelines regarding the surgical strategy to be adopted, thymectomy, IOPTH, cryopreservation, or AT of parathyroid tissue.

The aim of the present study is to evaluate the current trends of surgical management in RHPT using an online survey. The questions were designed to be easily answered, with only 10 to 15 min of time necessary to complete the questionnaire. To facilitate a better understanding, the survey was divided into six sections with three to eight questions each. Still, the study is limited as the survey was unable to cover all options of surgical details. Two participants remarked by email that their surgical strategy depends on factors such as status of kidney transplant, location of the glands, and blood supply. These details were not considered in the questionnaire.

The survey did not allow us to separately analyze different conditions of the patients such as predialysis, hemo- or peritoneal dialysis, and normal or impaired kidney graft function which have to be taken into account before planning the surgical strategy. The reason for a particular decision may also vary intraoperatively depending on the surgical findings. Considering different situations in the questions would have made the survey more complex and more difficult to understand. Selecting these questions thus reflects a deliberate compromise by referring to the most frequently encountered situations and strategies applied in patients with RHPT.

Table 4 Storage time of cryopreserved parathyroid tissue

Storage time	*n*	Percent
Less than 6 months	4	11.8
1 year	6	17.6
2–4 years	9	26.5
5 years	1	2.9
More than 5 years	14	4.2

n number of participants

Our international survey was supported by the presidents of the three societies invited to participate and was distributed to all society members. This way, a significant number of endocrine surgeons could be reached worldwide, and especially those working in Europe. Figure 2 shows the frequency of parathyroid surgery at the centers. To our knowledge, there are no international definitions of how many parathyroid surgeries per year characterize a "high-volume surgeon" or a "high-volume center." However, "high surgeon volume and specialization" are associated with an improved patient outcome, while "high hospital volume" appears to be of limited benefit [8].

Following extensive discussions, the consensus elaborated by the authorities of the German Association of General and Visceral Surgery specifies an annual rate of five and 25 procedures for hyperparathyroidism to qualify as a "competence center" or "reference center" for endocrine surgery, respectively [9]. Only two responders (2.3 %) participating in the current survey treat less than five patients per year surgically, and more than 75 % of the participants would fulfill the DGVA criteria of a "reference center." However, surgery in patients with RHPT is more complex than surgery in patients with PHPT. In endocrine surgery, the surgeon volume generally correlates inversely with complication rates. The lowest complication rates are achieved by surgeons performing at least 100 endocrine operations per year [10]. In particular, the surgeon's experience is a very important factor for good results in patients with RHPT [8].

Preoperative localization

Preoperative localization studies are not applied by 21 %. Gasparri et al. showed that preoperative sestamibi scintigraphy may be helpful, yet it is not essential in initial surgery [11]. However, hyperfunctioning ectopic and supernumerary glands can be detected preoperatively. As shown recently [12], ultrasonography and sestamibi scintigraphy, which showed a higher sensitivity than that of either ultrasonography or scintigraphy alone, led to the preoperative diagnosis of ectopic (29 %) or supernumerary parathyroid glands (10 %) and concomitant nodular thyroid disease (24 %).

Surgical strategy

As demonstrated in the current survey, there is no strong evidence in favor of one particular of the three "standard procedures" [4]. It has been shown that subtotal or total

parathyroidectomy with and without immediate AT, respectively, can be performed with comparable long-term results [13–17]. Analyzing 606 patients, Schneider et al. recently reported that all these procedures are feasible and safe with an effective decrease in calcium and PTH levels [16]. However, the authors critically discuss "subtotal (3½) parathyroidectomy" and remark that recurrent disease requires a neck re-exploration with a higher rate of morbidity. Total parathyroidectomy without immediate AT may result in adynamic bone disease. In a long-term follow-up, no patient developed adynamic bone disease in the series by Sadideen et al., and in only six (30 %) of 20 patients with functioning kidney grafts, permanent hypoparathyroidism was revealed 9 years after total parathyroidectomy without autografting [15]. Resection of sestamibi-positive glands only, as reported by one participant, is not recommended in patients on dialysis but may be chosen in individuals with mildly persisting RHPT following successful renal transplantation [18].

Thymectomy

Three fourths of responders in our survey perform transcervical thymectomy routinely during initial subtotal or total parathyroidectomy. Transcervical thymectomy results in a high yield of parathyroid tissue and seems essential to "cure" selected patients with various types of hyperparathyroidism [19].

However, even an extended cervical exploration including extirpation of at least four hyperplastic parathyroid glands, synchronously performed transcervical thymectomy, and central (level VI) neck dissection may postoperatively result in undetectable PTH levels in only 73.4 % of patients with RHPT (Burgstaller et al., submitted for publication). The Topar Trial [20], a prospective controlled multicenter study comparing total parathyroidectomy without AT and without thymectomy to total parathyroidectomy with AT and with thymectomy, may help to increase the evidence concerning the necessity of initial transcervical thymectomy in surgery for PHPT.

Intraoperative PTH monitoring

IOPTH was introduced to the surgical management of PHPT to exclude multiple gland disease and to confirm complete excision of hypersecreting tissue and thus intraoperative success. The short half-life of PTH and rapid PTH decrease within minutes after excision of a hypersecreting parathyroid gland made this tool feasible. Divergent interpretive models have been described in the literature [21, 22]. Due to an unequal pathophysiological background [23] in RHPT as compared with PHPT, the intraoperative interpretation of a significant PTH decrease to document a successful surgical procedure is less simple and depends on the surgical objectives informed by the patients' conditions (e.g., predialysis/dialysis/successful kidney graft). Furthermore, circulating non-(1–84)PTH fragments cumulate in patients with renal insufficiency and show cross-reactions to commercially available rapid PTH assays applicable for IOPTH. This may lead to "artificially high" PTH values and a prolonged PTH decline [23–25]. Consequently, IOPTH applying rapid intact PTH assays is not recommended for routine use in RHPT patients [24], as the intraoperative characteristics of intact PTH levels cannot predict early or long-term outcome [25, 26].

On the other hand, using a bio-intact PTH assay ("new-generation assay") may enable us to differentiate between "sufficient" and "insufficient" parathyroidectomy [24, 27]. Nevertheless, nearly half of the participants routinely use IOPTH with rapid intact PTH assays during RHPT. The intraoperative PTH curve influences the surgical strategy in 40 %. The reported interpretation criteria differ and show a wide degree of variation as a result of the unpredictably different PTH clearances in individual patients with various pathophysiological conditions.

Cryopreservation

Cryopreservation of parathyroid glands was first described by Wells et al. in 1974 [28]. Permanent hypoparathyroidism has a significantly negative impact on patients' quality of life. Replantation of cryopreserved autologous parathyroid tissue may restore normal PTH values and parathyroid metabolism. Cryopreservation of parathyroid glands is recommended especially when total parathyroidectomy without AT is performed and aparathyroidism is the consequence [4, 16]. Moreover, permanent hypoparathyroidism or inadequate parathyroid function may theoretically develop after leaving behind a parathyroid remnant (in the neck or forearm). Therefore, cryopreservation is also recommended after subtotal or total parathyroidectomy with immediate AT, respectively [16]. Still, only 40 % of the participants report to cryopreserve parathyroid tissue. Despite the frequent cases of hypoparathyroidism and in concordance with other studies [16], Borot et al. reported a replantation rate of only 1.6 % (22 of 1,376 samples) while analyzing data from nine French tissue banks [29]. Furthermore, 80 % of the implanted samples were nonfunctioning and only 10 % partially functioning. These disappointing results may be related to technical and logistic problems in less experienced centers [29]. In the analyzed group, no single implanted parathyroid tissue with a storage time of more than 1 year was shown to be functional [29]. Nevertheless, 24 responders (70.6 %) in this survey report a storage time of more than 1 year. Bacterial contamination was reported in up to 23 % of the samples [30], yet microbiological evaluation of the graft before implantation is only performed by the minority of the survey participants.

In contrast to immediate AT, 15 % of the participants report an onset of graft function within 48 h. No "early"

onset of graft functions is reported for cryopreserved tissue. Most participants identify the onset of function after more than 14 days of delayed autografting. Echenique Elizondo et al. reported an adequate parathyroid function after 5 weeks following immediate presternal subcutaneous AT [31]. In their national study, Borot et al. [29] found only two cryopreserved autografts (10 %) to be fully functional, two (10 %) to be partially functional, and 17 (80 %) to be nonfunctional at 26 months' median follow-up.

In contrast, the participants in this survey report much better results: 40.3 % of the patients needed no and 50.1 % a mild calcium substitution, respectively. The reasons for these divergences are unclear. In conclusion, cryopreservation and replantation of cryopreserved parathyroid tissue should exclusively be used in experienced centers [16, 29, 32]. As shown recently [33], delayed AT of cryopreserved tissue following parathyroid surgery in patients with RHPT effectively normalizes PTH and calcium levels in medically untreatable hypoparathyroidism. The success rate is high if an adequate cryopreservation procedure is applied [33, 34] and the duration of storage is no longer than 24 h [34]. However, delayed AT of cryopreserved parathyroid tissue is rarely necessary, as reported recently in a single-center study documenting the necessity in 15 (1.6 %) of 883 interventions only [33, 35].

Conclusions

In view of the drawbacks of such an international survey, it nevertheless reveals the vague situations and documents the lack of clear surgical recommendations in patients with RHPT and failed medical treatment. Altogether, the present survey with its divergent answers and different strategies applied in identical situations calls for international studies to acquire a better level of evidence. Cryopreservation seems rarely necessary, and the cryopreservation of parathyroid tissue as a rule should thus be questioned.

Acknowledgments The authors are particularly grateful to Alexander Klockhaus who, with his advanced programming skills, made this online survey feasible.

Conflicts of interest None.

Appendix: Questions in details

General questions

1	Country of your hospital	*TEXT (optional)*
2	Region	• *Africa* • *Asia* • *Australia* • *Europe* • *North America* • *South America*
3	City	*TEXT (optional)*
4	Institution	*TEXT (optional)*
5	How many parathyroid surgeries are performed in your hospital (average per year)?	• *< 10* • *10–30* • *30–50* • *50–100* • *> 100*
6	How many surgeries for RENAL hyperparathyroidism are performed in your hospital (average per year)?	• *< 10* • *10–30* • *30–50* • *50–100* • *> 100*

Preoperative localization

7	Which preoperative localization studies are routinely performed?	• *Ultrasound* • *99mTc-Sestamibi* • *CT* • *MRT* • *Other (TEXT)*

Surgical strategy

8	Which operation do you perform?	• *Subtotal (3 ½) parathyroidectomy* • *Total parathyroidectomy with autograft* • *Total parathyroidectomy without autograft* • *Excision only of the Sestamibi-positive gland(s)* • *Other (TEXT)*
9	If "Subtotal parathyroidectomy"—how many glands are left in situ?	• *½* • *1* • *1½* • *2* • *Other*
10	Immediate autotransplantation: location of graft	• *Forearm* • *Sternocleidomastoid muscle* • *Other*

11	Immediate autotransplantation: amount of tissue transplanted	• *___mg (TEXT)* • *___pieces (TEXT)*
12	Is transcervical thymectomy routinely performed?	• *Yes* • *No*
13	Is sternotomy performed in first operation?	• *Yes (routinely)* • *Only with positive localization* • *Never* • *Other (TEXT)*

Immediate autotransplantation during surgery for renal hyperparathyroidism

14	Is parathyroid autotransplantation performed?	• *Routinely* • *Depends on PTH monitoring* • *Only in patients before renal transplantation* • *Only in patients after renal transplantation* • *Other (TEXT)*
15	Location of implantation?	• *Forearm* • *Sternocleidomastoid muscle* • *Other (TEXT)*
16	Preparation of graft?	*TEXT*
17	Control of graft function?	• *Casanova test routinely* • *Blood samples from graft-arm* • *Serum PTH* • *Other (TEXT)*
18	Startup of graft function in most cases (from experience)?	• *0–24 h* • *24–48 h* • *48 h–4 days* • *4–7 days* • *7–14 days* • *14–30 days* • *>30 days*

Cryopreservation

19	Cryopreservation performed?	• *Routinely* • *Depends on PTH monitoring* • *Only in patients before renal transplantation* • *Only in patients after renal transplantation* • *Other (TEXT)*
20	Technique of cryopreservation?	*TEXT*
21	Storage time	• *6 months* • *1 year* • *2–4 years* • *5 years* • *>5 years*

Delayed autotransplantation of cryopreserved tissue

22	Indication for autotransplantation	• *Reoperation* • *Fresh graft failure* • *Hypoparathyroidism following total* • *Parathyroidectomy* • *Other (TEXT)*
23	How often was replantation necessary?	• *No replantation yet* • *1 patient* • *2–5 patients* • *5–10 patients* • *10–20 patients* • *>20 patients*
24	Location of replantation?	• *Forearm* • *Sternocleidomastoid muscle* • *Anterior tibial muscle* • *Presternal* • *Other (TEXT)*
25	Amount of tissue transplanted	• *___mg (TEXT)* • *___pieces (TEXT)*
26	Evaluation of graft before implantation?	*TEXT*
27	Postimplantation function control?	• *Basal serum PTH* • *Casanova test routinely* • *Blood samples from graft-arm vs.* • *Non-grafted arm* • *Other (TEXT)*
28	Results	• *No substitution necessary* • *Mild substitution* • *Recurrent disease in graft*

Intraoperative PTH- monitoring

29	IOPTH used?	• *Routinely* • *Only for scientifically reasons* • *Only for reoperations* • *Never*
30	Type of assay?	• Quick-intraoperative iPTH assay (Nichols Institute Diagnostics, San Juan Capistrano, CA, USA) • Immulite Turbo intact PTH assay (Diagnostic Products Corporation, Los Angeles, CA, USA) • Assay using Roche Elecsys analyzers (Roche Diagnostics, Indianapolis, IN, USA) • Future Diagnostics BV, Wijchen, the Netherlands
31	Time points	• *Before skin incision* • *Visualization of adenoma* • *Excision of a gland* • *5 min after excision* • *10 min after excision*

		• *15 min after excision*
		• *20 min after excision*
		• *25 min after excision*
		• *30 min after excision*
		• *Other (TEXT)*
32	Criterion used	• *≥50 % from highest value within 10 min*
		• *≥50 % from preincision value within 10 min*
		• *≥50 % from highest value within 15 min*
		• *≥50 % from highest value within 15 min and normal range*
		• *Other (TEXT)*
33	Influence on surgical strategy	• *Yes*
		• *No*
		• *IOPTH only gives "recommendations"*
		• *Other (TEXT)*

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