

A Prospective Study of the Factors Related to The Survival of Autologous Parathyroid Gland Left Brachioradialis Transplantation: A Single-Center Study and Long-Term Follow-Up

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1. Abstract

Parathyroid gland transplantation into the sternocleidomastoid muscle is effective, but it is not possible to confirm transplant survival with this method. In this study, we evaluated parathyroid autotransplantation into the brachioradialis muscle and evaluated the factors associated with short- (up to 6 months) and long-term survival (up to 3 years).

1.1. Objectives: To evaluate autologous parathyroid gland left forearm brachioradialis muscle transplantation and analyze the factors related to transplant survival.

1.2. Methods: We followed-up patients who underwent thyroidectomy and autologous parathyroid left forearm brachioradialis muscle transplantation in our center from September 2013 to January 2018. all enrolled patients underwent at least 3 years of follow-up. We calculated the transplant survival rate at several time points and analyzed the factors related to survival.

1.3. Results: We evaluated 238 transplanted cases, for which the long-term survival rate was 85.7% (204/238), and the short-term survival rate was 86.1% (205/238). Sixty-five cases had two parathyroid glands transplanted into the left forearm brachioradialis muscle. The long-term survival rate was 92.3% (60/65), and the short-term survival rate was 95.4% (62/65). Survival was not related to age, sex, surgical method, preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone concentration, or preoperative serum calcium. The lowest serum calcium within 48 hours after surgery may be an

independent predictor of transplant survival; lower serum calcium was associated with higher survival probability. However, the difference in serum calcium values between patients with not- vs long-term parathyroid gland transplant survival was small, and further research is needed.

1.4. Conclusions: The lowest serum calcium concentration within 48 hours after surgery may predict transplant survival. we recommend appropriate calcium supplementation. The word “appropriate” does not refer to the specific blood calcium value, but rather to supplementation according to the patient’s symptoms, and to supplementing as little as possible or even not at all.

2. Introduction

Thyroidectomy is the main cause of hypoparathyroidism [1, 2], with an incidence ranging from 0.0% to 20.2% [3]. Generally, permanent injury is considered if function is not restored within 6–12 months [4]. The symptoms of permanent hypoparathyroidism and calcium ion dysregulation may persist long-term, and hypocalcemia symptoms should be considered a medical emergency. Adequate recognition and management is needed to decrease morbidity and costs [5].

Thyroidectomy causes decreased parathyroid function in approximately 75% of cases [6]. To prevent hypoparathyroidism after thyroidectomy, the American Thyroid Association Surgical Affairs Committee released a statement providing an overview of its recommendations regarding diagnosis, prevention, and treatment, in 2018. The statement pointed out that the fine anatomy of the dorsal

thyroid membrane preserves the surface of the thyroid and the adipose tissue adjacent to the parathyroid glands, which helps protect the blood supply to the parathyroid glands. After identifying the parathyroid glands during thyroidectomy, the parathyroid blood supply should be evaluated and a decision made regarding whether to autotransplant to preserve as much functional parathyroid gland as possible [7].

The transplantation site is usually the sternocleidomastoid muscle. However, there is no way to confirm whether the transplanted parathyroid glands are functional and whether the transplanted parathyroid glands survive, using this method. Parathyroid gland reimplantation in forearm subcutaneous tissue during thyroid surgery is safe, easy, and effective; furthermore, this method solves the problem of assessing post-transplantation function [8].

In this study, autologous parathyroid glands were transplanted into the forearm brachioradialis muscle. Postoperatively, we compared the serum parathyroid hormone concentrations in the cephalic veins of bilateral elbows to confirm whether the autologous transplanted parathyroid glands were functional. Transplant survival rate and the general clinical data were recorded for all patients with a follow-up period of more than 3 years. We analyzed the factors affecting the transplant survival rate to improve the survival rate of parathyroid forearm transplantation.

3. Methods

3.1. Patients

We reviewed patients who underwent thyroidectomy and left forearm parathyroid gland transplantation in our center from September 2013 to January 2018. Each patient received one or two parathyroid gland transplants in the left forearm. All enrolled patients were followed-up for at least 3 years. On the first day, 1 month, 2 months, 6 months, 1 year, and 3 years after the operation, we measured the parathyroid hormone concentration in blood samples taken from the cephalic veins in the left and right elbows of each patient. Parathyroid hormone concentration ratios in the transplanted arm/non-transplanted arm > 1.5 [9,10] indicated successful transplantation. We then analyzed the following as possible factors associated with transplant survival: age, sex, operation method, preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone, preoperative serum calcium, and lowest blood calcium concentration within 48 hours after surgery. We considered the first day, 1 month, and 2

months after the operation as the short-term. Parathyroid hormone concentration ratios in the transplanted arm/non-transplanted arm > 1.5 at one of the three time points was considered to indicate successful transplantation, and survival to 6 months, 1 year, and 3 years was considered long-term survival. Ratios > 1.5 at one of the three time points was considered successful transplantation.

3.2 Transplantation Method

Before surgery, our team of doctors explained the condition and surgical risks to the patients and their families. Hypoparathyroidism is a major risk of thyroidectomy. We explained this clearly to the patient and their family members and obtained consent before surgery. We also discussed that it is possible to perform parathyroid gland transplantation during the operation. If the patient and family members agreed with our plan that the transplant site would be the left side, we performed parathyroid transplantation in the left forearm. Five surgeons experienced in thyroid surgery and parathyroid transplantation performed the transplantations. If a good blood supply to the parathyroid gland could not be guaranteed during the operation or because of miscutting and other reasons, parathyroid gland transplantation was performed. The first step was to remove a small section of the parathyroid gland and perform snap-frozen pathology. The assistant cut the remaining suspected parathyroid tissue into small pieces, mixed it with normal saline, and aspirated the mixture into a syringe. Once the intraoperative frozen pathology indicated that the tissue was parathyroid gland (within 30 minutes), the mixture was immediately implanted in the brachioradialis muscle of the left forearm. The specific operation method is to use a scalpel to cut the transplanted parathyroid glands into 1-mm sections in a stainless steel basin and mix the sections with isotonic sodium chloride solution (0.3–0.5 mL) (Figure 1). The suspension is then aspirated with a 1-mL syringe, and the contents are then injected into the brachioradialis muscle of the left forearm through the 1-mL syringe with a 20-G needle positioned 1–1.5-cm from the outer side of the forearm and 5 cm from the elbow. The patient's skin is pinched with the operator's index finger and thumb, and the needle is inserted approximately 1.5 cm while ensuring that the needle tip enters the muscle. Saline (0.5 mL) is then aspirated into the same syringe and injected to release any tissue sections remaining in the syringe (Figure 2) [11]. If the transplantation is of the second parathyroid gland, intraoperative pathological verification is still required.



Figure 1: Parathyroid transplantation syringe



Figure 2: The point of parathyroid transplantation

3.3. Perioperative Evaluation and Follow-Up

Before surgery, we measured basal parathyroid hormone concentration, serum calcium concentration, preoperative hemoglobin, and preoperative albumin. Parathyroid hormone concentrations were measured from blood samples taken from the cephalic veins at bilateral elbows on the first day, 1 month, 2 months, 6 months, 1 year, and 3 years after the operation. Blood calcium concentrations

24 hours and 48 hours after the operation were also measured. The normal ranges for serum calcium and parathyroid hormone concentrations are 2.25–2.75 mmol/L and 15–65 ng/L, respectively. Serum calcium concentrations were measured using an automatic analyzer (Toshiba Medical Systems, Tochigi-ken, Japan), and a Cobas E601 was used for automatic washing (Hitachi High-Technologies, Tokyo, Japan) to measure serum parathyroid hormone

concentrations [11]. Blood calcium monitoring was performed 24- and 48 hours after the operation, and the lowest blood calcium was recorded. Calcium gluconate intravenous infusion was used when muscle twitching or spasm was observed after surgery. Permanent hypoparathyroidism was considered if there were no signs of transplant function 6 months after surgery [7].

4. Statistical Method

Statistical analysis was performed using SPSS 22.0 statistical software (IBM Corp., Armonk, NY). Measurement data conforming to a normal distribution were expressed as mean \pm standard deviation, and comparisons between groups were analyzed using the independent sample's t test. Numerical data were expressed as rate or composition ratio, and we used the chi-square test for comparisons between groups. We also performed multivariate logistic regression analysis to study the factors influencing transplant survival.

5. Results

A total of 238 patients were enrolled in this study. Of the 238 cases, 11 had benign thyroid tumors, 10 had nodular goiter, 1 had an adenomatous nodule, and the remaining 227 had thyroid malignancies, of which 226 were papillary thyroid carcinomas, and 1 was medullary thyroid carcinoma. No patients developed an inflammatory response at the graft site of the left forearm. (Table 1) shows the transplant survival rates. The long- and short-term survival rates were 85.7% (204/238) and 86.1% (205/238), respectively. One month after surgery, most of the transplanted parathyroid glands had survived, with a survival rate of 73.5% (175/238). Among these cases, 65 cases had two parathyroid glands implanted in the brachioradialis muscle of the left forearm, and the short- and long-term survival rates were 95.4% (62/65) and 92.3% (60/65), respectively (Table 2).

Table 1: Transplant Survival Rates at Each Follow-up Point

	Number of survivors	Total number of participants	Survival rate (%)
1 day	29	238	12.2
1 month	175	238	73.5
2 months	179	238	75.2
6 months	172	238	72.3
1 year	169	238	71
3 years	173	238	72.7
Long-term survival	204	238	85.7
Short-term survival	205	238	86.1

1 day means whether it is functional, not whether it is survival.

Table 2: Survival rate after implanting two parathyroid gland transplants

	Number of survivors receiving two transplants	Total number of patients receiving two transplants	Survival rate (%)
1 day	13	65	20
1 month	52	65	80
2 months	55	65	84.6
6 months	50	65	76.9
1 year	48	65	73.8
3 years	55	65	84.6
Long-term survival	60	65	92.3
Short-term survival	62	65	95.4

1 day means whether it is functional, not whether it is survival.

5.1. Analysis of Factors Related To Long-Term Transplant Survival

Transplant survival 6 months, 1 year, and 3 years postoperatively was considered long-term survival, and a parathyroid hormone concentration ratio > 1.5 between the left and right elbows at the three time points was considered successful transplantation. Of the 238 total cases, transplants failed in 34 cases, and were successful in 204 cases. Nine and 37 transplants failed and survived, respectively, in men, and 25 and 167 transplants failed and survived, respectively, in women ($P = 0.255$). The average age of the transplant failure group was 44.41 ± 10.46 years, while the average age of the successful transplantation group was 45.42 ± 11.03 years. One patient in the failure group and five patients in the successful transplantation group had diabetes mellitus ($P = 0.691$). Five patients in the failure group and 27 patients in the successful transplantation

group had hypertension (Table 3; $P = 0.816$). Regarding differences in the surgical methods, 102 cases did not undergo bilateral thyroidectomy, and 87 of these underwent successful parathyroid gland transplantation. Seventy-four cases underwent bilateral total thyroidectomy with or without unilateral central area lymph node dissection, of which 64 cases underwent successful parathyroid gland transplantation. Sixty-two cases underwent bilateral total thyroidectomy plus bilateral central area lymph node dissection, of which 53 cases achieved transplant survival. There was no statistical difference between the surgical methods ($P = 0.974$).

Preoperative hemoglobin and preoperative albumin in the transplant failure and transplant success groups were 13.57 ± 1.34 and 13.43 ± 1.5 g/dl, respectively, and 44.94 ± 2.93 and 44.96 ± 2.74 g/l, respectively. Preoperative parathyroid hormone and preoperative serum calcium in the transplant failure and transplant success

groups were 44.95 ± 14.56 and 43.34 ± 15.66 ng/l, respectively, and 2.4 ± 0.12 and 2.42 ± 0.11 mmol/l, respectively. The lowest blood calcium in the transplant failure and transplant success groups within 48 hours after operation was 1.98 ± 0.18 and 1.99 ± 0.18 mmol/l, respectively.

Multivariate regression analysis of the factors associated with transplant survival identified no statistical difference for age, sex,

surgical method, preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone, and preoperative serum calcium. However, we found a statistically significant difference for the lowest blood calcium within 48 hours after surgery, which was negatively correlated with transplant survival; lower blood calcium concentrations were associated with higher transplant survival rates (Table 3).

Table 3: Factors related to long-term parathyroid gland transplant survival

	Failed transplantation (n=34)	Successful transplantation (n=204)	t/χ ²	P
Sex (Male/Female)	9/25	37/167	1.298	0.255
Surgical approach			0.053	0.974
Unilateral lobectomy	15	87		
Bilateral lobectomy 1	10	64		
Bilateral lobectomy 2	9	53		
Diabetes (yes/no)	Jan-33	5/199	0.028	0.866
Hypertension (yes/no)	29-May	27/177	0.054	0.816
Age	44.41±10.46	45.42±11.03	-0.498	0.619
Preoperative hemoglobin	13.57±1.34	13.43±1.5	0.521	0.603
Preoperative albumin	44.94±2.93	44.96±2.74	-0.043	0.966
Preoperative parathyroid hormone	44.95±14.56	43.34±15.66	0.56	0.576
Preoperative serum calcium	2.4±0.12	2.42±0.11	-1.004	0.316
48-h minimum blood calcium	1.98±0.18	1.99±0.18	-0.17	0.865

S.E., standard error; OR, odds ratio; CI: confidence interval

	β	S.E.	Wald	P	OR (95%CI)
Sex (control: female)	-0.325	0.668	0.236	0.627	0.723 (0.195, 2.677)
Surgical approach (control: unilateral lobectomy)					
Bilateral lobectomy 1	0.161	0.527	0.093	0.76	1.174 (0.418, 3.297)
Bilateral lobectomy 2	-0.253	0.607	0.173	0.677	0.777 (0.236, 2.554)
Diabetes (yes/no)	-0.076	1.251	0.004	0.951	0.926 (0.08, 10.756)
Hypertension (yes/no)	-0.102	0.627	0.026	0.871	0.903 (0.264, 3.086)
Age	0.008	0.021	0.161	0.688	1.008 (0.968, 1.051)
Preoperative hemoglobin	-0.081	0.19	0.18	0.671	0.922 (0.635, 1.339)
Preoperative albumin	0.001	0.083	0	0.993	1.001 (0.851, 1.177)
Preoperative parathyroid hormone	-0.006	0.013	0.24	0.624	0.994 (0.969, 1.019)
Preoperative serum calcium	1.445	2.114	0.467	0.494	4.243 (0.067, 267.428)
48-h minimum blood calcium	-14.355	6.834	4.412	0.036	0 (0, 0.383)

Remarks: Bilateral lobectomy 1: Bilateral thyroidectomy with or without unilateral central area lymph node dissection. Bilateral lobectomy 2: Bilateral thyroidectomy with bilateral central area lymph node dissection.

5.2. Short-Term Survival with No Long-Term Survival

Some transplants survived in the short term (ratio > 1.5 at least once on the first day, 1 month, and 2 months after the operation), but they did not survive long-term (ratio < 1.5, 6 months, 1 year, and 3 years after the operation).

The number of transplants surviving short-term in the 238 cases was 205, of which 194 survived both short- and long-term, and 11

survived short-term but not long-term. Univariate and multivariate analysis showed that transplant survival was related to age, sex, and surgical method. There were no statistically significant differences in preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone, preoperative serum calcium, and lowest blood calcium within 48 hours after surgery. The rate of transplants surviving short-term but not long-term was 5.37% (11/205), as shown in (Table 4).

Table 4: Analysis of the factors related to short-term survival with no long-term survival of parathyroid gland transplants

	Short- and long-term survival (n=194)	Short-term survival and no long-term survival (n=11, 5.37%)	t/χ ²	P
Sex (Male/Female)	34/160	4/7	2.446	0.118
Surgical approach			0.071	0.965
Unilateral lobectomy	82	5		
Bilateral lobectomy 1	60	3		
Bilateral lobectomy 2	52	3		
Diabetes (yes/no)	5/189	1-Oct	0.107	0.743
Hypertension (yes/no)	25/169	9-Feb	0.002	0.963
age	45.33±11.17	46.73±11.23	-0.404	0.687
Preoperative hemoglobin	13.42±1.5	14.16±0.83	-1.611	0.109
Preoperative albumin	45±2.71	45.79±2.53	-0.95	0.343
Preoperative parathyroid hormone	43.16±15.49	50.12±21.48	-1.418	0.158
Preoperative serum calcium	2.42±0.11	2.41±0.09	0.221	0.826
48-h minimum blood calcium	1.98±0.17	1.97±0.18	0.228	0.82

	β	S.E.	Wald	P	OR(95%CI)
Sex (control: female)	0.108	1.061	0.01	0.919	1.114 (0.139, 8.921)
Surgical approach (control: unilateral lobectomy)					
Bilateral lobectomy 1	-0.606	0.934	0.421	0.517	0.546 (0.087, 3.404)
Bilateral lobectomy 2	-1.117	1.152	0.939	0.332	0.327 (0.034, 3.133)
Diabetes (yes/no)	1.428	1.438	0.985	0.321	4.169 (0.249, 69.887)
Hypertension (yes/no)	-0.208	1.117	0.035	0.852	0.812 (0.091, 7.246)
Age	0.006	0.034	0.032	0.859	1.006 (0.94, 1.076)
Preoperative hemoglobin	0.365	0.346	1.114	0.291	1.44 (0.732, 2.834)
Preoperative albumin	0.072	0.148	0.234	0.628	1.074 (0.803, 1.437)
Preoperative parathyroid hormone	0.008	0.02	0.15	0.698	1.008 (0.969, 1.047)
Preoperative serum calcium	-3.001	3.973	0.571	0.45	0.05 (0, 119.662)
48-h minimum blood calcium	4.916	9.616	0.261	0.609	136.461 (0, 2.09e10)

S.E., standard error; OR, odds ratio; CI: confidence interval

Bilateral lobectomy 1: Bilateral thyroidectomy with or without unilateral central area lymph node dissection; Bilateral lobectomy 2: Bilateral thyroidectomy with bilateral central area lymph node dissection.

5.3. No Short-Term Ability to Produce PTH, With Long-Term Survival

Some transplants did not regain the ability to produce PTH short-term but did so long-term. We did not perform the relevant analyses for this group as the sample size was too small to perform multivariate analysis or correlation analysis.

6. Discussion

For patients undergoing unilateral thyroidectomy in the first operation, even if all parathyroid glands on the surgical side are inactivated, because the contralateral parathyroid glands are preserved, parathyroid gland function will compensate, and it is true that permanent hypoparathyroidism will not occur. However, if the patient's tumor recurs, and the contralateral thyroid gland needs to be removed in a second operation, if the parathyroid glands on the side of the first operation are no longer active, the parathyroid glands on the side of the second operation may be transplanted. However, if the transplant does not survive, the patient will develop permanent hypoparathyroidism. In contrast, if the patient's parathyroid transplant survives the first surgery by autologous transplantation, the second surgery has no associated hypoparathyroidism risk. Therefore, whether the surgery is bilateral or unilateral, the parathyroid glands lacking blood supply need to be transplanted.

Currently, no specific technique can guarantee that the parathyroid glands will not be damaged or that hypoparathyroidism will not occur with thyroid surgery. Most researchers advocate that the blood supply to the parathyroid glands should be protected as much as possible during the operation. For miscut parathyroid glands, auto transplantation of the glands can effectively reduce the risk of hypoparathyroidism. In 1926, Lahey performed parathyroid auto transplantation after thyroid surgery for the first time to prevent postoperative hypoparathyroidism [12]. Since then, parathyroid transplantation technology has developed. Palazzo et al. performed parathyroid auto transplantation in more than 1000 cases of total thyroidectomy. The postoperative hypoparathyroidism incidence rate was < 1% [13]. stated that if at least one parathyroid gland is transplanted after thyroid surgery, postoperative hypoparathyroidism will not occur [14].

The first-choice reimplantation site is the sternocleidomastoid muscle. believe that this muscle has the characteristics of rich blood flow and high oxygen concentration [15]. The advantage of this method is that an additional skin incision is not required, and the disadvantage is that it is impossible to verify transplant survival. Parathyroid autologous forearm transplantation solves this shortcoming, and Cavallaro et al. published a series of reports on

this technique [8, 16]. The authors transplanted parathyroid glands into 2–3 subcutaneous tissues of the non-dominant forearm. The survival rate was as high as 90%, and the authors believe that this technique is safe and effective. Compared with other parathyroid replantation techniques, the main advantage is that transplant function can be assessed during follow-up, and it is simple and easy to implement. This technique can be applied to all potential patients undergoing thyroidectomy; however, the number of cases undergoing this procedure remains low, follow-up times have been short, and the factors associated with transplant survival have not been studied [8, 16].

In this study, we evaluated a larger number of cases, used a longer follow-up time, and performed a preliminary study of the factors related to transplant survival, namely age, sex, operation method, preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone, preoperative serum calcium, and lowest blood calcium within 48 hours after surgery.

The ideal transplant site should meet three conditions: (1) high local oxygen partial pressure; (2) high degree of peripheral vascularization; and (3) immune preferential zone [17].

Higher hemoglobin concentrations are associated with stronger oxygen-carrying capacity [18]; therefore, different hemoglobin concentrations affect the local partial pressure of oxygen. We hypothesized that hemoglobin may be an influencing factor in parathyroid transplant survival, but our results showed that preoperative hemoglobin concentration was not associated with long-term transplant survival.

Age, sex, preoperative albumin concentrations, diabetes, or hypertension create different internal environmental and metabolic states. Therefore, these factors may also affect parathyroid gland transplant survival; however, our results showed that none of these factors was associated with transplant survival. We also speculated that different surgical methods, preoperative parathyroid hormone concentration, and preoperative serum calcium also affect transplant survival to a certain extent; however, we found no correlation.

Research has shown that calcium can regulate the growth of proliferative parathyroid cells [19-21]. In this study, we observed that long-term parathyroid survival was statistically different according to the lowest blood calcium within 48 hours after surgery, and there was a negative correlation; lower blood calcium was associated with higher transplant survival rates. Therefore, we concluded that low serum calcium concentrations in the early postoperative period may stimulate the functional recovery of autologous parathyroid glands. However, the difference in minimum 48-hour serum calcium values between patients whether the parathyroid gland transplant was successful was small. The reason for this phenomenon may be that some patients have low-calcium symptoms within 48 hours after thyroidectomy, and we im-

mediately provide intravenous and oral calcium supplementation to improve the patients' symptoms. This calcium supplementation may be the reason why the minimum 48-h blood calcium value did not differ greatly between patients with not- vs long-term parathyroid gland transplant survival. Therefore, we speculate that the success of parathyroid gland transplantation may be related to the lowest serum calcium at 48 hours, and we recommend appropriate calcium supplementation. The word "appropriate" does not refer to the specific blood calcium value, but rather to supplementation according to the patient's symptoms, and to supplementing as little as possible or even not at all. However, further research is needed.

In this study, the overall long-term transplant survival rate was 92.3% (60/65), which is a satisfactory result. We hypothesize that if three transplants are implanted, the survival rate will be higher. If four transplants are implanted, the transplant survival rate should be close to 100% because each transplanted parathyroid gland is independent, and the probability that none of the four parathyroid glands would survive is quite low.

This transplantation method also has other advantages. For example, for those requiring a second operation, the probability of hypoparathyroidism is 30% [22]. If survival of the previous forearm transplant is clear before surgery, there is minimal worry regarding hypoparathyroidism when performing subsequent lymph node dissection, if necessary. If it is clear that transplantation was unsuccessful, the surgeon should choose a more suitable surgical method (relatively more conservative) before the operation, and pay more attention to protecting the blood supply of the parathyroid gland during the operation. There is no need for preventive lymph node dissection, which may increase the risk of damaging the parathyroid glands. Surgeons should fully communicate with patients and their families before surgery to inform them that the risk of permanent hypoparathyroidism is relatively high.

We also found that some transplanted parathyroid glands survived short-term but not long-term, and some transplanted parathyroid glands did not survive short-term but survived long-term. We are still studying why these two conditions occurred.

7. Conclusions

The results of this prospective study showed that autologous parathyroid forearm brachioradialis muscle transplantation is safe and effective. The long-term survival rate of a single parathyroid gland transplantation was 85.7%, and the long-term survival rate of two parathyroid glands was 92.3%. We suggest that parathyroid glands with poor blood supply found during the operation can be directly transplanted into the left forearm brachioradialis instead of the sternocleidomastoid muscle.

We found that age, sex, surgical method, preoperative hemoglobin, preoperative albumin, diabetes, hypertension, preoperative parathyroid hormone, and preoperative serum calcium did not affect the transplant survival rate. However, the lowest blood calcium

within 48 hours after surgery may be an independent factor influencing transplant survival, although further research is needed. For patients undergoing parathyroid auto transplantation, we recommend avoiding excessive exogenous calcium supplementation after thyroid surgery in the absence of obvious symptoms, which may improve the long-term survival rate of transplanted parathyroid glands. In a second operation, the surgeon can choose the best surgical plan according to whether the previous parathyroid forearm transplant survived. The principle is to avoid or reduce the occurrence of permanent hypoparathyroidism and ensure the radical cure of the thyroid tumor as much as possible.

References

- Melikyan AA, Menkov AV. Postoperative Hypoparathyroidism: Prognosis, Prevention, and Treatment (Review). *Sovrem Tekhnologii Med.* 2020; 12: 101-8.
- Hakami Y, Khan A. Hypoparathyroidism. *Front Horm Res.* 2019; 51: 109-26.
- Harsløf T, Rolighed L, Rejnmark L. Huge variations in definition and reported incidence of postsurgical hypoparathyroidism: a systematic review. *Endocrine.* 2019; 64: 176-83.
- Caglià P, Puglisi S, Buffone A. Post-thyroidectomy hypoparathyroidism, what should we keep in mind? *Ann Ital Chir.* 2017; 6: 371-81.
- Dedivitis RA, Aires FT, Cernea CR. Hypoparathyroidism after thyroidectomy: prevention, assessment and management. *Curr Opin Otolaryngol Head Neck Surg.* 2017; 25: 142-6.
- Clarke BL, Brown EM, Collins MT. Epidemiology and diagnosis of hypoparathyroidism. *J Clin Endocrinol Metab.* 2016; 101: 2284-99.
- Orloff LA, Wiseman SM, Bernet VJ. American Thyroid Association Statement on postoperative hypoparathyroidism : diagnosis, prevention, and management in adults. *Thyroid.* 2018; 28: 830-41.
- Cavallaro G, Iorio O, Centanni M. Parathyroid Reimplantation in Forearm Subcutaneous Tissue During Thyroidectomy: A Simple and Effective Way to Avoid Hypoparathyroidism. *World J Surg.* 2015; 39: 1936-42.
- Saxe A. Parathyroid transplantation: a review. *Surgery.* 1984; 95: 507-26.
- Lo CY, Tam SC. Parathyroid autotransplantation during thyroidectomy: documentation of graft function. *Arch Surg.* 2001; 136: 1381-5.
- Zhang D, Gao L, He G, Chen J, Fang L. Predictors of graft function after parathyroid autotransplantation during thyroid surgery. *Head Neck.* 2018; 40: 2476-81.
- Lahey FH. The transplantation of parathyroids in partial thyroidectomy. *Surg Gynecol Obstet.* 1926; 62: 508-9.
- Palazzo FF, Sywak MS, Sidhu SB. Parathyroid autotransplantation during total thyroidectomy--does the number of glands transplanted affect outcome?. *World J Surg.* 2005; 29: 629-31.
- Zedenius J, Wadstrom C, Delbridge L. Routine autotransplantation of at least one parathyroid gland during total thyroidectomy may reduce permanent hypoparathyroidism to zero. *Aust N Z J Surg.* 1999; 69: 794-7.
- Zimmermann H, Zimmermann D, Reuss R. Towards a medically approved technology for alginate-based microcapsules allowing long-term immunoisolated transplantation. *J Mater Sci Mater Med.* 2005; 16: 491-501.
- Cavallaro G, Iorio O, Centanni M. Parathyroid reimplantation with PR-FaST technique in unselected patients during thyroidectomy. A case series with long term follow up confirming graft vitality and parathormone production. *Int J Surg.* 2017; 39: 202-5.
- Cao L, Wang L. Current status and trend of parathyroid transplantation. *CHINESE JOURNAL OF PRACTICAL SURGERY.* 2008; 28: 227-9.
- Antwi-Bafour S, Hammond S, Adjei JK. A case-control study of prevalence of anemia among patients with type 2 diabetes. *J Med Case Rep.* 2016; 10: 110.
- Fukagawa M, Kitaoka M, Fukuda N, Yi H, Kurokawa K. Pathogenesis and management of parathyroid hyperplasia in chronic renal failure: role of calcitriol. *Miner Electrolyte Metab.* 1995; 21: 97-100.
- Tanaka Y, Funahashi H, Imai T. Functional and morphometric study of cryopreserved human parathyroid tissue transplanted into nude mice. *World J Surg.* 1996; 20: 692-9; discussion 698-9.
- Sakaguchi K. Acidic fibroblast growth factor autocrine system as a mediator of calcium-regulated parathyroid cell growth. *J Biol Chem.* 1992; 267: 24554-62.
- Guerrero MA. Cryopreservation of parathyroid glands. *Int J Endocrinol.* 2010; 2010: 829540.