

A Cross-sectional Study of Nipple and Areola Sensation after Female to Male Subcutaneous Mastectomy Comparing between Semicircular, Concentric Circular and Free Nipple Graft Techniques

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Background: Subcutaneous mastectomy is one of the most common procedure in Female to Male transsexualism. The sensitivity of nipple-areola-complex (NAC) postoperatively is still unclear.

Objective: To evaluate nipple-areola-complex (NAC) sensation after female to male subcutaneous mastectomy comparing between semicircular, concentric circular and free nipple graft techniques.

Materials and Methods: The present study included 47 patients who underwent subcutaneous mastectomy (MG) with semicircular (SC, n=6), concentric circular (CC, n=17) and free nipple graft technique (FNG, n=24). NAC sensitivity was assessed for touch, pain, cold temperature, erogenous sensation and nipple erection.

Results: The most sensation patients concerned is touch sensation (58%), pain (18%), erogenous/erection (8%) and cold (7%). For touch sensation SC and CC still had touch sensation but 27% of FNG had loss touch sensation ($p=0.001$). For pain sensation SC and CC still had touch sensation but FNG had lost pain 33% at areola and 23% at nipple ($p<0.001$). For cold sensation 12% of CC and 25% of FNG had lost cold sensation at areola ($p<0.001$) and 12% of CC and 9% of FNG had lost cold sensation at nipple ($p<0.001$). For erogenous sensation 50% of SC, 35% of CC and 77% of FNG had lost erogenous sensation. For nipple erection 50% of SC, 35% of CC had erect but no nipple erection in FNG.

Conclusion: All sensation parameters of NAC. SC is better than CC and FNG is the worst. The most sensation patients concerned is touch sensation.

Keywords: Nipple and areola sensation; Female-to-male subcutaneous mastectomy; Free nipple graft; Nipple sensation; Subcutaneous mastectomy

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Subcutaneous mastectomy is one of the first steps in sexual reassignment in female-to-male transsexuals (FTMTS). The main goal is to masculinize the chest by removing breast tissues and skin excessive and proper reduction and reposition nipple and areola, obliteration of inframammary fold (IMF) and to minimize chest wall scar⁽¹⁾. Chest surgery in transmen also differs from mastectomy for cancer prophylaxis or treatment. Specifically, relatively thick adipocutaneous flaps aid to mitigate contour deformities

and necessitate a dissection plane different from oncologic mastectomy. That's why transmen should be counseled to continue with appropriate breast cancer screening⁽²⁾. There are 5 techniques of subcutaneous mastectomy based on size of breasts, grade of ptosis, skin elasticity, nipple reduction and acceptable to scar. Semicircular, transareolar, concentric circular, extended concentric circular and free nipple graft. Semicircular techniques is suitable for small size breasts (A-B cup) with good elasticity, Concentric circular technique is suitable for medium size (B cup) with good skin elasticity or small breast with ptosis grade I-II while free nipple graft is suitable for large (C or larger cup), grade II-III ptosis with poor skin elasticity⁽³⁾.

In Monstrey study, postoperative NAC sensation is reduced which are more pronounced in patient with free nipple graft. We knew that blood flow into graft at 48 hours after grafting. The recipient nerve use basal lamina infrastructure of degenerated blood vessels and schwann cell of donor to grow⁽⁴⁾. Waris et al⁽⁵⁾ study reinnervation of human full thickness skin graft using cholinesterase method, 3 in 8 patients, aged 3 months to 13 year old, after 3 weeks of grafting found both dermal and subepidermal nerve plexi, around some hair follicle, sweat gland and erector pilli via

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under graft and margin of the grafts, orient toward denervated graft area in random fashion. Fiber transmit perception of only gross (touch, pain, temperature) sensation but not more sophisticated epicritic (light touch, vibration, two-point discrimination sensation)⁽⁶⁾. Some study result regeneration of sensation occur following order: pain, touch, cold, warmth. Sensation improve with time but never completely recover⁽⁷⁾ and, the major contribution to graft reinnervation was via subdermal route than marginal⁽⁸⁾.

In clinical study of Patel et al with 56 patients underwent subcutaneous mastectomy with FNG, the number of individuals saying they had no sensation or a little bit postoperatively decreased from 66.67% to 61.54% to 38.89%, at 1, 3, and 6 months respectively. Additionally, the individuals with quite a bit or normal nipple sensation postoperatively increased from 16.67%, to 23.08%, to 22.22% from 1 to 3 to 6 months respectively⁽⁹⁾. In Knox et al study, at 2 months postoperative, 47% of patient underwent CC had partial sensation while 90% of patient underwent FNG were still no any sensation⁽¹⁰⁾. Nelson study 12 patients underwent FNG did a questionnaire at mean follow-up 10 months. 7 in 12 patients (58%) had returned nipple sensation with three of them had normal sensation⁽¹¹⁾. Wolter study of nipple sensation at 1 year postoperatively of liposuction SC, CC and FNG, 50% of total patients underwent semicircular and 53% of total that underwent concentric circular showed very good sensation while FNG was no data collected⁽¹²⁾.

NAC sensation result from special peripheral sensory receptor which connect to specific intercostal nerve. According to glabrous peripheral sensory receptor which had divided to myelinated supplied mechanoreceptor, thermal, noxious and to unmyelinated C fiber supplied pain, cold, heat, light touch and autonomic. NAC also has erogenous sensation⁽¹³⁾. There are two types of erogenous sensation: nonspecific type and specific. Nonspecific type as in normal skin the nerve supplying composed of usual density as dermal nerve network. The pleasure sensation come from exaggerate tickle. The specific type found in mucocutaneous region such as clitoris, prepuce, lip, nipple. The more organized nerve tissue rises higher in dermis than normal skin. Each organ appear to be identical. They found Winkelman's mucocutaneous end organ (dense loops of nonmyelinated nerve fiber in whorls shape supplied by two to six myelinated nerve) in subpapillary dermis. It is apparent that the mass of smooth muscle and glandular-duct tissue in the nipple and areola serves to block normal development of the dermal-nerve networks seen in other erogenous regions. The nipple is well innervated immediately below the epidermis, but the glandular and smooth-muscle structures crowd out the uniform richness of middle dermal networks and prevent development of special end organs^(14,15). In MRI study support result that nipple stimulation increase signal of medial paracentral lobe which a genital sensory cortex⁽¹⁶⁾.

The 3rd to 5th intercostal nerve which divided to anterior and lateral innervation contribute to sensitivity of

nipple areolar complex (NAC). Most frequently cited is 4th lateral cutaneous branch which 93% from deep branch and 7% from superficial branch and medial innervation from 3rd and 4th superficial anterior cutaneous branch. Deep branch penetrate fascia of serratus muscle, runs along the pectoralis major muscular fascia then runs inferomedially before turning upward to penetrate the breast gland and innervate the nipple at base. Superficial branch runs at subcutaneous layer and innervate areola at 1 to 4 o'clock for right breast and 8 to 11 o'clock for left breast

In histological study, there are robust nerve at base of nipple and proceeding forward to the tip along the milk duct. There are few nerves at the sides of nipple and practically none in the areola except very loosely some around galactophores in Montgomery tubercles and muscle fiber and there are only sensory nerve. Smooth muscle fiber in the nipple and areola arranged in radial toward nipple and circular, so contraction reduce the surface of areola and cause the nipple to raise. Smooth muscle contraction in respond to cold, tactile and psychic stimuli. These response for two major biological function: making milk available for infant and serving as visual and tactile sex releasers⁽¹⁹⁾.

To our knowledge, no study has quantitatively analyzed the relationship of NAC sensation between these 3 techniques. Therefore, we undertook this study to assess the sensitivity of the NAC at least postoperative 6 months between three techniques.

Materials and Methods

The study protocol for single-center, cross-sectional, nonrandomized control trial was approved by the Ethics Committee of Ramathibodi Hospital (No. MURA2020/413). All protocols followed the ethic guidelines of declaration and all participants signed an informed consent form. The study was carried out between November 2019 to March 2020.

The total of 225 patients were selected from a Division of Plastic and Maxillo-facial Surgery, Ramathibodi Hospital. We collected patients done subcutaneous mastectomy from March 2016 to August 2019 by single surgeon. We exclude 179 patients who can not contact or uncomfortable to follow-up at out patient unit and both total necrosis of NAC. Total 71 patients were allocated in 4 groups: group 1 consist of women who done subcutaneous mastectomy with semicircular technique (SC, n=6), group 2 with concentric circular technique (CC, n=17), group 3 with free nipple graft (FNG, n=24) and group 4 is control group (CG, n=24) which were an inpatients female with no history of breast surgery or breast disease. All 4 groups, we exclude if patients had uncontrolled diabetic, active collagen vascular disease, alcoholism, neurological impair; impair sensation of abdominal wall; history of chemotherapy or radiation at breast or abdomen; pregnancy or breast feeding less than 1 year.

In all groups, Skin sensitivity test were performed by same examiner in a quiet environment. During the test, patients take off clothes and lay on comfortable bed. Areola

was measured for width and length. Then, the areola was divided in four quadrants and nipple is an additional point, for total of five regions. Reference region is a skin of upper abdomen at the same side of NAC tested, around 8 cm in vertically below NAC (Figure 1). In each region, three sensory modalities were tested in sequence: touch, pain and cold temperature compare to reference point (Figure 2A-C).

For sensitivity to touch, We use Semmes-Weinstein filament, corresponding to threshold/potential skin pressure values of 0.07 (normal), 0.4 (normal), 2 (diminish light touch), 4 (diminish protective touch), 10 (loss of protective touch) and 300 (deep pressure sensation only) g/mm². Patients was asked to close their eyes. The monofilament was used to exert pressure until bent and maintained for 5 seconds as recommended⁽²⁰⁾. The perceived touch value was recorded.

For pain sensation, We used 2 sharp stick touch for 1 seconds at NAC and reference points at the same time. We allow force at midline. For cold temperature, we used 1 cm² of metal touched with ice pack for 5 seconds and placed on skin for 2 seconds. All test were compared to the reference point ipsilaterally and report in 4 levels: no feeling,

mild, same, hypersensitivity compare to reference point.

Nipple was asked for erogenous sensation and was reported in 4 groups: no, partial, normal and hypersensitivity compared to preoperative. Last, nipple was asked for erection or not.

For the result of each person, we use “median” for represent all 8 quadrants of areola and both nipples.

Statistical analysis

Data were analyzed using STATA version 14.1 program. For categorical variables were evaluated using the Fisher’s exact test. Data are presented as number (percent). For continuous variables compared using Kruskal-Wallis test. Data are presented as median (IQR). A p-value <0.05 was considered statistically significant.

Results

All 71 patients completed the study. Four groups were matched for age (CG: median 32 years (29 to 37.5); SC: median 33.5 years (32 to 35); CC: median 31 years (26 to 32); FNG: median 32 years (30 to 38)), underlying disease and smoking (Table 1). FNG had the most BMI (p=0.006). There are significantly different in areola size which FNG was the smallest (median 18 cm x 25 cm, p<0.001 (Table 2). No significant difference of graft loss, keloid and widening scar between techniques (Table 3). Median follow-up for SC was 16 months, CC 8 months and FNG 15 months (Table 4). The most important sensation that patient concerned is touch (58%), then pain (18%), erogenous or erection (8%) and cold temperature (7%) respectively (Figure 3). For touch sensation (Figure 4), all techniques have touch sensation at NAC after follow-up. At areola, 30% of FNG diminish to loss protective touch sensation (p<0.001). At nipple, 24% of CC show diminish light touch (p<0.001) and FNG were different from CG with 19% of FNG show diminish protective touch sensation and 27% show loss of protective touch sensation (p=0.001). For pain sensation (Figure 5), at areola, 33% of FNG had no pain sensation (p<0.001). At nipple, 12% in CC had mild pain sensation (p=0.04) and 23% of FNG had no pain sensation with 55% of FNG had mild pain sensation (p<0.001). For cold sensation (Figure 6), at areola, 12% of CC had no cold sensation (p=0.006) and 25% of FNG had no cold sensation (p<0.001). At nipple, 17% of SC had mild cold sensation while 41% of CC had mild and no cold sensation and 77% of FNG had mild and no cold sensation (p<0.001). For erogenous sensation (Figure 7), 4% in CG had no erogenous sensation. All technique can lost erogenous sensation with statistic significant (50% of SC, 35% of CC and 77% of FNG). We still found 23% of FNG have erogenous sensation. For nipple erection (Figure 8), in CG, nipple erection was mostly found 96% while nipple can erect only 50% in SC, 35% in CC and we found that FNG, nipple can not erect at all. Comparison of nipple and areola (Table 4, Figure 3 to 6), nipple was more hypersensitivity in every aspects of sensations. The conclusion of all sensations compare between technique was in Figure 9.

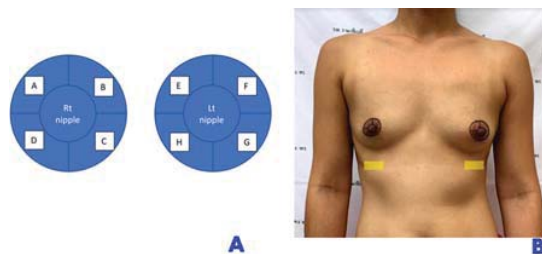


Figure 1. A) A to G corresponding to four areola quadrants in right and left NAC. B) Yellow marks are reference point at 8 cm below NAC.

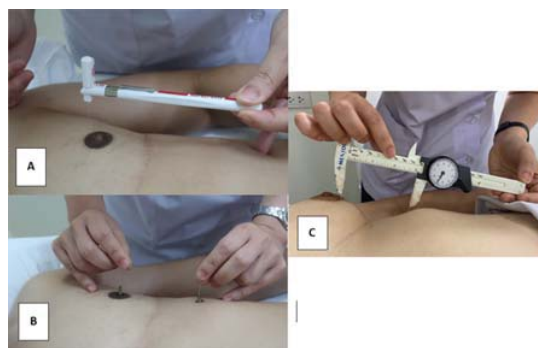


Figure 2. Sensation test in sequence. A) Test for touch sensation. B) Test for cold temperature sensation, C) Test for pain sensation.

Table 1. Demographic data

Patient demographics	Control (n=24)	Semicircular (n=6)	Concentric circular (n=17)	Free nipple graft (n=24)	p-value
Age (years), median (IQR)	32 (29 to 37.5)	33.5 (32 to 35)	31 (26 to 32)	32 (30 to 38)	0.270
BMI (kg/m ²), median (IQR)	22.05 (19.7 to 24.5)	24.5 (22.2 to 25.3)	21.5 (19.8 to 23.9)	24.55 (21.7 to 30.65)	0.006*
Underlying, n (%)					
No	14 (58)	5 (83)	13 (76)	18 (75)	0.56
Yes	10 (42)	1 (17)	4 (24)	6 (25)	
Smoking, n (%)					
No	24 (100)	6 (100)	16 (94)	23 (96)	0.99
Active	0 (0.0)	0 (0.0)	1 (6)	1 (4)	

Boldfaced p-value denote statistical significance (p<0.05)

* Comparison of groups by the Kruskal-Wallis test Data are presented as median (IQR).

Comparison between control group with SC,CC, FNG by Fisher's exact test Data are presented as number (%).

Table 2. Size of areola

Patient demographics	Semicircular (n=6)	Concentric circular (n=17)	Free nipple graft (n=24)	p-value
Size of areola median (IQR)				
Width (mm)	22 (21 to 25)	22.5 (20 to 25)	18 (16.5 to 20)	<0.001*
Length (mm)	30 (29.5 to 33)	30 (27 to 35)	25 (22 to 27.5)	<0.001*

Table 3. Complications after surgery

Complications, n (%)	Semicircular (n=6)	Concentric circular (n=17)	Free nipple graft (n=24)	p-value
Total =10 (21.2)	0 (0)	6 (35)	4 (17)	0.185
Graft loss/flap necrosis	0 (0.0)	0 (0.0)	2 (8.3)	0.440
Keloid	0 (0.0)	2 (11.8)	1 (4.2)	0.372
Widening scar	0 (0.0)	4 (35.3)	1 (4.2)	0.001*

Boldfaced p-value denote statistical significance (p<0.05)

* Comparison of groups by Fisher's exact test Data are presented as number (%).

Table 4. Follow-up times (months)

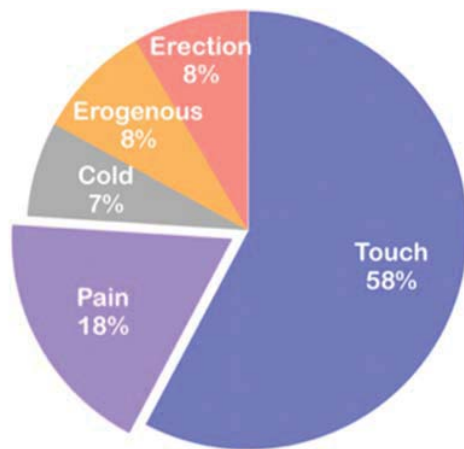
Follow-up times (months)	Semicircular (n=6)	Concentric circular (n=17)	Free nipple graft (n=24)	p-value
Follow-up times (months): median (min, max)	16 (5, 29)	8 (4, 26)	15 (6, 46)	0.031*

* Comparison of groups by the Kruskal-Wallis test Data are presented as median (range).

Discussion

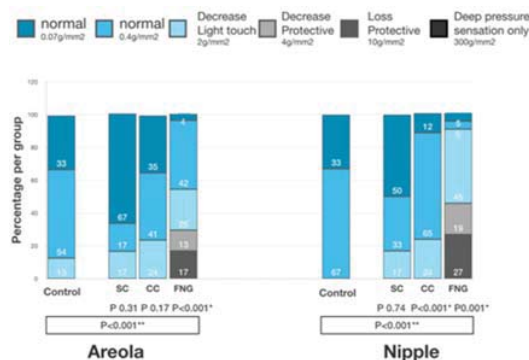
Semicircular technique is first described by Webster⁽²¹⁾ in 1946. The advantage are concealed scar confine to lower half areola. Disadvantage is small window

for work, making excision tissue and hemostasis challenging. Concentric circular technique is first described by Davidson⁽²²⁾ in 1979. The advantage are (1) allow areola reduction and remove skin excess (2) concealed scar to circumareola (3)



Boldface p-value denote statistical significance ($p < 0.05$)
 * Comparison of group by Fisher's exact test Data are presented as number (%).

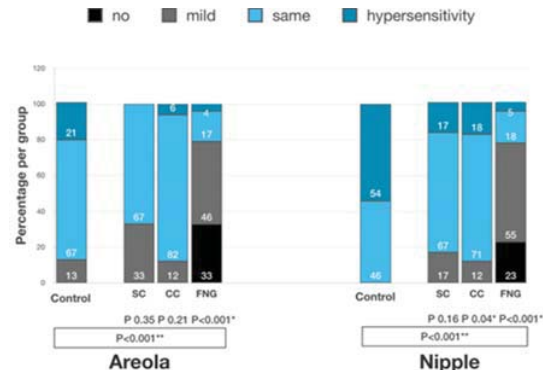
Figure 3. Priority of sensation patient concerned.



Boldface p-value denote statistical significance ($p < 0.05$)
 * Comparison of groups by Random effect ordinary logistic regression. Data are presented as number (%).
 ** Comparison between group with SC, CC, FNG by Random effect ordinary logistic regression.

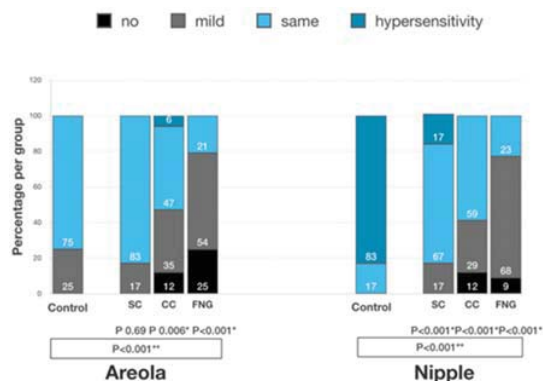
Figure 4. Touch sensation.

good exposure for excision or hemostasis. Free nipple graft technique is described by Thorek⁽²³⁾. Advantage of free nipple graft technique are: (1) excellent exposure, stop hemostasis and more rapid resection of tissue, (2) nipple reduction, and (3) areola resizing and repositioning. Disadvantages are the long residual scars and NAC pigmentary and sensory change. Timing of return sensation of NAC after surgery and types of sensation change were still not clear in data. To our knowledge, our study is the first to attempt to quantify sensation in the nipple and areola between 3 techniques.



Boldface p-value denote statistical significance ($p < 0.05$)
 * Comparison of groups by Random effect ordinary logistic regression. Data are presented as number (%).
 ** Comparison between group with SC, CC, FNG by Random effect ordinary logistic regression.

Figure 5. Pain sensation.



Boldface p-value denote statistical ($p < 0.05$)
 * Comparison of groups by Random effect ordinary logistic regression. Data are presented as number (%).
 ** Comparison between group with SC, CC, FNG by Random effect ordinary logistic regression.

Figure 6. Cold sensation.

In the present study, the Semmes-Weinstein method was used to evaluate cutaneous pressure sensitivity. Area of bias include variation between examiners and product maintenance, to minimize bias, we took care of equipment, used in proper application techniques and converted measurement into grams using manufacture's protocol. A single examiner performed all the tests. This technique has the advantage of being reproducible, affordable, easy to learn and not require specific technology.

Normal size of areola in mens is 20x27 mm⁽²⁴⁾. In our study of areola size, 3 techniques are quite similar

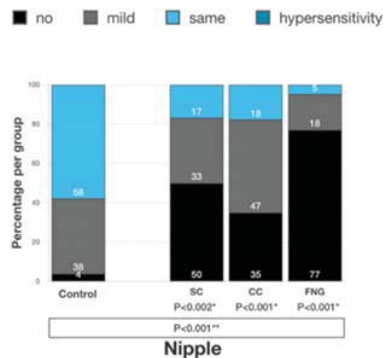


Figure 7. Erogenous sensation.

Boldfaced p-value denote statistical significance ($p < 0.05$)
 * Comparison of groups by Random effect ordinary logistic regression. Data are presented as number (%).
 ** Comparison between group with SC, CC, FNG by Random effect ordinary logistic regression.

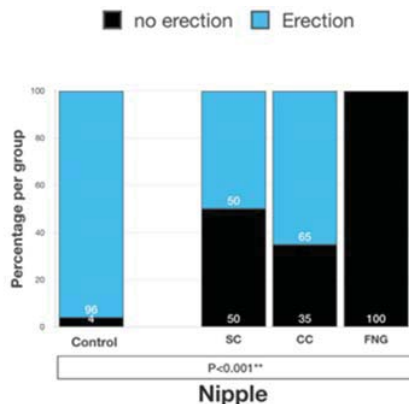


Figure 8. Nipple erection.

Boldfaced p-value denote statistical significance ($p < 0.05$)
 ** Comparison of groups by Fisher's exact test. Data are presented as number (%)

to average areola size in men which FNG is the smallest. There was no any data about priority of NAC sensation.

Previous study, we found study of NAC sensation mostly in female with breast reduction. For imply information of sensation and nipple erection. Our finding corroborate to those of author. Craig and Sykes⁽²⁵⁾ found sensitivity to pain and light touch were less than 50% of nipples in free grafting, but in over 80% when the nipple was left with the gland. None of FNG had nipple erection. O'Connor⁽²⁷⁾ return sensation to the areola at 3 to 4 months, and to the nipple at 6 months after surgery but they did not believe for erogenous sensation to FNG. In contrast to our study, Townsend⁽²⁸⁾ found erectile function in more

Technique		Nipple	Areola
SC	Touch		
	Pain		
	Cold		
	Erogenous	50%	
	Erection	50%	
CC	Touch		
	Pain		
	Cold	12%	12%
	Erogenous	35%	
	Erection	35%	
FNG	Touch		
	Pain	23%	33%
	Cold	9%	25%
	Erogenous	75%	
	Erection	100%	

The number show n (%) that has no any sensation.

Figure 9. Conclusion of sensation between techniques.

than 70% of FNG, and good sensation in two thirds. Ahmed et al⁽²⁹⁾ compare FNG and inferior pedicle mastectomy at least 1 year postoperative which 2 to 3 mm thick at areola and 5 to 6 mm thick at nipple. FNG areola touch sensation (35 g/m²) is similar to inferior pedicle while in nipple (25.7 g/m²), inferior pedicle is superior (13.4 g/m²) and subjective asseessment report worse sensation only 1/21 of inferior pedicle and 4/17 of FNG. Their erogenous sensation and erection found 90% of inferior pedicle and 58% of FNG.

There are small previous study sensation of NAC in female-to-male subcutaneous mastectomy, Patel et al⁽⁹⁾ with 56 patients done FNG, 61% improve sensation at 6 month postoperation. In Knox et al⁽¹⁰⁾, at 2 months postoperative, 47% of patient done CC had partial sensation while 90% of patient done FNG were still no any sensation. Nelson⁽¹¹⁾ 12 patients done FNG at mean follow-up 10 months. 58% have returned nipple sensation with 25% had normal sensation. Wolter⁽¹²⁾ of nipple sensation at 1 year postoperatively of liposuction SC, CC and FNG, 50% of total patients done semicircular and 53% of total that done concentric circular show very good sensation while FNG is no data collected.

For all aspects of sensations, in our results, semicircular is better than concentric circular and FNG subcutaneous mastectomy is the worst (Table 11). We assume a reason is in semicircular technique, there are dermo-parenchymal nipple pedicle which contain of superficial cutaneous nerve while in concentric circular and FNG, dissection of tissue are more prone to injury to nerve. All 3 techniques have at least pressure sensation, we assume that because pressure receptor (Pacian corpuscle) are located in deep dermis which deeper than other receptor so regeneration of nerve reach first.

According to complication, previous study, hematoma is the most frequent complication⁽³⁰⁾.

McEvenue⁽³¹⁾ comparing semicircular with liposuction and DIFNG. Total complication 18% which DIFNG have less seroma (4.3% vs. 18.3%) and hematoma (3.8% vs. 10.6%) compare to semicircular in statistic significant. Monstrey study⁽³⁾ reoperation hematoma is also the most (9.8%), was more frequent in transareolar (20%) and semicircular (6.6%) compared to concentric circular (1.4%) and FNG (2.7%). Cregten⁽³²⁾, comparing between SC, CC pedicle nipple and FNG, reoperation rate 5% which FNG are least than other group. Results was same as in study of Tim⁽³³⁾. In our study of 47 patients, no any hematoma or seroma developed.

Our study has some weak points. We did not record the women's hormonal cycles which could influence not only NAC sensitivity, but also sexual function. Our follow-up period of at least 6 months, findings undoubtedly would be stronger if we had a longer follow-up. However, many times is very difficult to follow-up with patients from a public health service for a longer time. The non-randomized design and the small sample size which should be considered for further study.

Conclusion

After at least 6-month postoperative, all sensation parameters of NAC after female-to-male subcutaneous mastectomy, SC is better than CC and FNG is the worst. The most sensation patients concerned is touch sensation. Nipple has more hypersensitivity compare to areola in all parameters. FNG has no nipple erection but still had 25% of erogenous sensation. We can use these information to counsel for preoperative information.

What is already known on this topic?

Subcutaneous mastectomy is the most common procedure in sexual reassignment in female to male transsexuals. The techniques of mastectomy is depend on breast size, nipple position, ptosis of breast tissue and skin laxity. The sensation of nipple areolar complex after mastectomy is still unclear.

What this study adds?

Evaluation of nipple-areola-complex (NAC) sensation after female to male subcutaneous mastectomy in aspect of touch, pain, cold, erogenous and nipple erection postoperatively comparing between semicircular, concentric circular and free nipple graft techniques.

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Potential conflicts of interest

The authors declare no conflict of interest.

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