



Quantitative assessment and risk factors for nipple–areolar complex malposition after nipple-sparing mastectomy

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Abstract

Purpose Nipple sparing mastectomy (NSM) for breast cancer preserves the nipple–areola complex (NAC) and has limited the extent of the scar, giving good cosmetic results. However, NAC malposition may occur. The aim of this study is to evaluate NAC malposition after NSM and to determine factors associated with malposition in two-stage reconstruction.

Methods The subjects were 46 patients who underwent unilateral NSM, without contralateral mastopexy or reduction surgery, in two-stage reconstruction using an expander with implant or flap replacement. Vertical and horizontal NAC malposition and predictors of malposition were evaluated before and more than 1 year after reconstruction surgery.

Results The total amount of saline injected into the expander and aging were significant predictors of increased superior malposition of NAC before and more than 1 year after reconstruction or implant surgery. In contrast, the amount of saline injected into the expander until 2 weeks after expander insertion was a significant predictor of decreased superior NAC malposition. BMI was also a statistically significant predictor of decreased superior NAC malposition, but this result was likely to have been due to the measurement method. Autologous reconstruction was a significant negative predictor of superior malposition at more than 1 year after surgery. Superior NAC malposition resulting from full expansion of the expander improved by a mean vertical angle of 4.5° after autologous reconstruction, but hardly improved after implant use. In autologous reconstruction, NAC tended to move slightly to the lateral side after autologous reconstruction, compared to implant use.

Conclusions Until 2 weeks after expander insertion, as much saline as possible should be injected to prevent superior NAC malposition. At full expansion, superior malposition of vertical angle >4.5° may require repositioning surgery.

Keywords Nipple-sparing mastectomy · Nipple–areolar complex · Nipple · Malposition

Introduction

Nipple-sparing mastectomy (NSM) is an increasingly common surgery for breast cancer. Preservation of the native nipple–areola complex (NAC) and limiting the extent of the scar are desired by many women to attain a good cosmetic

result [1–6]. However, malposition of NAC is relatively common after NSM, and this can be a challenging issue that may require repositioning surgery [7–10]. A two-stage procedure using a tissue expander is common in implant reconstruction [11], and we also often perform a two-stage approach in flap reconstruction, with transplant of a de-epithelialized flap following insertion of a tissue expander. This avoids the patchwork-like scar around the skin paddle of the flap that shows that the breast has been reconstructed [12].

A few reports have shown that autologous reconstruction has less NAC malposition compared to implant surgery [13, 14]. However, conversely, a recent study found that autologous reconstruction is a risk factor for NAC malposition [9]. This issue is unclear because few studies have compared implant and autologous reconstruction [9] or evaluated NAC malposition quantitatively [16]. To the best of our knowledge, implant and autologous reconstruction have not been compared using the same quantitative method, and

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risk factors for NAC malposition have been incompletely evaluated. Furthermore, in two-stage procedures, it is not clear how malposition of NAC after adequate expansion of the expander with saline changes (or does not change) after implant or flap replacement surgery.

The aims of this study are to evaluate NAC malposition quantitatively and identify factors associated with malposition in two-stage reconstruction following NSM. We also evaluated how malposition after expansion of the expander with saline changed after the second stage of implant or flap surgery. A better understanding of the risk factors and NAC changes might improve the indication for NSM and prevent NAC malposition. Furthermore, predicting a need for repositioning surgery might enable this surgery or contralateral mastopexy/reduction surgery to be performed concurrently with the second-stage surgery, and thus eliminate the need for additional surgery.

Patients and methods

The study was performed as a nonrandomized, retrospective cohort study, and thus, was granted exemption from institutional Clinical Ethics Committee approval (no. 1297). Between August 2014 and January 2017, a total of 126 Japanese patients with breast cancer underwent two-stage reconstruction using an expander and implant or flap replacement at the Department of Plastic and Reconstructive Surgery and Breast and Endocrine Surgery, Gunma University Hospital. A total of 46 patients who underwent unilateral NSM without contralateral mastopexy or reduction surgery and had a follow-up period of more than a year after the second-stage surgery were included in the study. These patients included 23 who underwent autologous reconstruction and 23 who received implant surgery with a latissimus dorsi flap ($n = 13$) or a transverse rectus abdominis myocutaneous (TRAM) flap or a deep inferior epigastric perforator flap ($n = 10$). All expanders and breast implants were placed in a submuscular (sub pectoralis major muscle) pocket. No acellular human dermis was used due to the restrictions of the Japanese health insurance system. Thirteen flaps were placed in a submuscular pocket and 10 were placed in a subcutaneous pocket, which was separately made in the flap insertion. Textured type expanders were used in all patients. An anatomical cohesive gel implant (Allergan) was used in all except one of 23 implants. A round type implant was used in one case. Thirty-seven patients underwent immediate tissue expander indwelling with NSM and this procedure was delayed in 9 patients. We placed a few 3–0 absorbable sutures to stitch the posterior border of the nipple on the area of the pectoralis major muscle corresponding to the proper position marked preoperatively in a sitting or upright

position, if the pectoralis major muscle was present at the proper position.

Front-view photographs were used for evaluation of the nipple position. Vertical and horizontal malposition were evaluated using photographs taken just before and more than 1 year after the second-stage surgery. Vertical malposition was evaluated as the angle [which we refer to as the vertical angle (VA)] between the perpendicular line from the unaffected nipple to the midline and a line drawn from the unaffected nipple to the affected nipple (Fig. 1a). The more superior NAC moves, the greater the VA. The horizontal distance (HD) was defined as the perpendicular line from the nipple to the midline. The HD ratio (HDR) was defined as HD on the affected side/HD on the unaffected side, and was used as a measure of horizontal malposition (Fig. 1b) [16]. The more laterally NAC moves, the greater the HDR. To correct for natural asymmetry, HDR is presented as HDR divided by the preoperative (before NSM) HDR, and VA as VA minus the preoperative (before NSM) VA in patients who underwent immediate tissue expander indwelling surgery.

Data were collected for age, body mass index (BMI), saline solution injected into the expander (total amount injected, and amount injected until 2 weeks after expander insertion), autologous reconstruction (vs. implant), and primary (vs. delayed) expander insertion. Multivariate analysis using a stepwise multiple linear regression model was used to identify factors associated with NAC malposition. Mann–Whitney U test was used to compare implant reconstruction with autologous tissue. All data were analyzed using SPSS ver. 24 (Chicago, IL, USA). $p < 0.05$ was considered to be statistically significant.

Results

The mean age was 48.2 (range 37–76) years, the mean BMI was 22.4 (16.3–29.0) kg/m^2 , and the mean follow-up period was 23.4 (12–40) months. Radiation therapy was performed in only one patient. Complications in expander insertion surgery occurred in 8 patients with seroma, 2 with infection, none with hematoma, and 1 with exposure. A latissimus dorsi flap was successfully used for the exposure case. No other expanders required explantation during expansion.

The mean VAs showing superior malposition of the NAC just before and more than 1 year after autologous tissue or implant insertion were $8.2^\circ \pm 3.9^\circ$ (range 2.1° – 19.7°) and $6.0^\circ \pm 3.8^\circ$ (0.0° – 13.7°), respectively, and the mean VA change was $-2.1^\circ \pm 3.2^\circ$ (-10.5° to $+3.6^\circ$). The mean HDRs at the same time points were $1.05^\circ \pm 0.12^\circ$ (0.78° – 1.27°) and $0.98 \pm 0.10^\circ$ (0.78° – 1.19°), respectively, and the mean HDR change was $-0.07^\circ \pm 0.12^\circ$ (-0.31° to $+0.26^\circ$) (Table 1).

Significant predictors of NAC malposition identified by multiple regression are shown in Tables 1 and

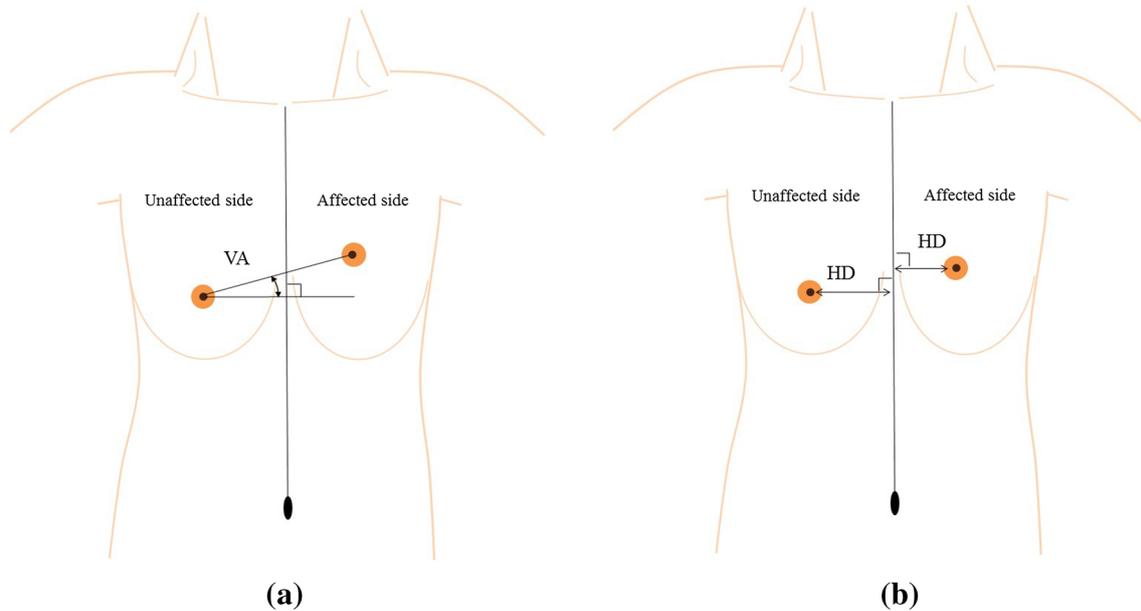


Fig. 1 **a** Vertical malposition was evaluated as the angle [which we refer to as the vertical angle (VA)] between the perpendicular line from the unaffected nipple to the midline and a line drawn from the unaffected nipple to the affected nipple. **b** The horizontal distance

(HD) was defined as the perpendicular line from the nipple to the midline. The HD ratio (HDR) was defined as HD on the affected side/HD on the unaffected side, and was used as a measure of horizontal malposition

Table 1 Vertical angle (VA) and horizontal distance ratio (HDR) just before and more than 1 year after the second-stage surgery, changes in VA and HDR, and significant predictors of NAC malposition in linear multiple logistic regression analysis

Item	Just before flap or implant insertion (B)	More than 1 year after flap or implant insertion (A)	Change (A – B)
Vertical angle (VA)	8.2 ± 3.9	6.0 ± 3.8	– 2.1 ± 3.3
Significant predictors of superior malposition	(Increase)	(Increase)	(Increase)
	Aging***	Aging***	–
	Total amount of injected saline***	Total amount of injected saline***	–
	(Decrease)	(Decrease)	(Decrease)
	Amount of injected saline until 2 weeks after expander insertion**	Autologous reconstruction***	Autologous reconstruction***
	BMI*	Amount of injected saline until 2 weeks after expander insertion**	
		BMI*	
Horizontal distance ratio (HDR)	1.05 ± 0.12	0.98 ± 0.10	– 0.07 ± 0.12
Significant predictors of horizontal (lateral) malposition	(Increase)	(Increase)	(Increase)
	–	Autologous reconstruction*	–
	(Increase)	(Decrease)	(Decrease)
	–	–	–

Mean ± SD

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

2. Significant regression equations were found for VA just before ($F = 10.38$, $p < 0.001$, $R^2 = 0.51$) and more than 1 year ($F = 14.70$, $p < 0.001$, $R^2 = 0.653$) after the second surgery, and for the difference in VA ($F = 68.20$,

$p < 0.001$, $R^2 = 0.613$) (Table 2). The total amount of saline injected into the expander and aging were significant predictors of an increased VA before and after the second surgery, whereas the amount of saline injected

Table 2 Significant predictors of vertical angle (VA) from a multiple linear regression model

Item:	Just before autologous or implant reconstruction (B)			More than 1 year after flap or implant insertion (A)			Change (A – B)		
	B	SE B	β	B	SE B	β	B	SE B	β
Aging	0.30	0.07	0.55***	0.30	0.06	0.58***	n.s.	n.s.	n.s.
BMI	–0.40	0.19	–0.33*	–0.33	0.15	–0.28*	n.s.	n.s.	n.s.
Injected saline into expander									
Total amount	0.02	0.01	0.77***	0.02	0.00	0.58***	n.s.	n.s.	n.s.
Amount until 2 weeks after expander insertion	–0.04	0.01	–0.35*	–0.03	0.01	–0.32**	n.s.	n.s.	n.s.
Autologous reconstruction (vs. implant)	–	–	–	–4.03	0.72	–0.54***	–4.98	0.60	–0.78***
Immediate expander (vs. delayed)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
R^2	0.51			0.65			0.61		
F	10.38***			14.70***			68.20***		

B partial regression coefficient, SE B standard error of partial regression coefficient, β standardized partial regression coefficient, R^2 adjusted coefficient of determination

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, n.s. not significant

into the expander until 2 weeks after expander insertion and BMI were significant predictors of a decreased VA. Autologous reconstruction was also a significant negative predictor of NAC malposition at more than 1 year after the surgery. Vertical NAC malposition just before the second surgery was improved more by autologous tissue reconstruction than by implant surgery (Tables 1, 2).

For HDR, a significant regression equation was found only at more than 1 year after autologous tissue or implant insertion ($F = 6.02$, $p = 0.018$, $R^2 = 0.123$), and the prediction accuracy was low based on the coefficient of determination. In autologous reconstruction, NAC tended to move slightly to the lateral side than after implant use (Table 1). A comparison of VA and HDR between autologous and implant reconstruction is shown in Table 3. The vertical NAC malposition after expansion with saline was improved by a mean of 4.50° after autologous reconstruction. While, it was not improved after implant surgery (worsen only by a mean of 0.23°).

Discussion

The NSM technique has the advantages of preservation of the native NAC and limiting the extent of the scar, resulting in a good cosmetic result [1–6]. However, NAC malposition significantly decreases the value of NSM [7]. Various techniques of NAC repositioning have been reported [8, 9], but the surgery is sometimes challenging and may produce an additional amount of scar. Therefore, it is important to evaluate causes of NAC malposition and identify risk factors for its occurrence.

In this study, the independent predictors of superior NAC malposition after two-stage reconstruction were the total amount of saline injected into the expander and aging. Total saline is significantly associated with mammary size, and aging is linked to breast ptosis. Therefore, our results support previous findings that suggested that breast ptosis [15, 16] or a large volume [7, 16] affect malposition. In contrast, the amount of saline injected until 2 weeks after expander insertion was a negative predictor of malposition. As Mori et al. reported, excess skin occurs with NSM, and overlying

Table 3 Vertical angle (VA) and horizontal distance ratio (HDR) compared between autologous and implant reconstruction

Item	Just before autologous or implant insertion (B)		More than 1 year after autologous or implant insertion (A)		Change (A – B)	
	Autologous	Implant	Autologous	Implant	Autologous	Implant
VA for NAC malposition (mean \pm SD)	8.63 \pm 4.60	7.70 \pm 3.12	4.13 \pm 3.35	7.92 \pm 3.18	–4.50 \pm 2.65	0.23 \pm 1.60
Mann–Whitney U test	$p = 0.62$		$p < 0.001$ ***		$p < 0.001$ ***	
HDR for NAC malposition (mean \pm SD)	1.08 \pm 0.12	1.03 \pm 0.12	1.02 \pm 0.09	0.95 \pm 0.09	–0.06 \pm 0.14	–0.08 \pm 0.10
Mann–Whitney U test	$p = 0.173$		$p = 0.012$ *		$p = 0.939$	

* $p < 0.05$, *** $p < 0.001$

mastectomy skin flaps will naturally begin to contract during the latency period of expansion [16]. In expander insertion, it is necessary to inject as much saline as possible, and our result supports the suggestion that as much as expansion as early as possible after expander insertion surgery might prevent superior malposition.

A few reports have suggested that NAC distortion and malposition are increased following reconstruction with implants compared with autologous tissue [13, 14], whereas another study found that autologous reconstruction was a risk factor for NAC malposition [7]. Autologous tissue reconstruction was a negative independent predictor of superior malposition of NAC in our study, and the mean VA at full expansion was improved by 4.5° after autologous tissue reconstruction and worsen only by 0.23° after implant surgery. This suggests that superior NAC malposition of $>4.5^\circ$ at full expansion may require repositioning surgery or contralateral mastopexy or reduction surgery, even if autologous tissue reconstruction is used. Peeling the skin off the pectoralis major muscle is likely to be one of the causes of improvement of NAC superior malposition. In this study, 10 of the 23 autologous reconstructions were placed in a subcutaneous pocket (on the pectoralis major muscle), which was separately made in the flap insertion, and 13 cases were placed in a submuscular pocket, where the TE was inserted. VAs in the subcutaneous and submuscular cases were $3.14^\circ \pm 1.30^\circ$ and $4.89^\circ \pm 4.23^\circ$, respectively, at more than 1 year after autologous insertion. Superior NAC malposition in flap insertion into a subcutaneous pocket was less than that for a submuscular pocket. Improvement of VA after flap insertion surgery into a subcutaneous pocket was also larger than that using a submuscular pocket (-5.37 ± 2.93 vs. -3.83 ± 2.30). These results show that, in autologous reconstruction, peeling the skin off the pectoralis major muscle can improve NAC superior malposition. For this reason,

in recent two-stage reconstructions using autologous tissue, we have inserted all flaps into subcutaneous pockets. However, even if flaps were inserted into a submuscular pocket, VA improved more than with implant reconstruction (-3.83 ± 2.30 vs. 0.23 ± 1.60), which suggests that peeling the skin off the pectoralis major muscle was not the only reason for improvement of malposition. The softness and mobility of autologous reconstruction may cause improvement of upper NAC, which is more influenced by gravity.

A previous article reported that BMI was a risk factor for NAC malposition in a study using implant reconstruction only [13], whereas a recent report showed that BMI was not a predictor of NAC repositioning [9]. In our study, BMI was a negative predictor of superior malposition. This result might be due to our evaluation method, since a larger BMI tends to be related to a larger width of the chest wall. In patients with wide and slender chest walls, but with the same superior malposition, VA would be lower in the patient with the wider chest wall. This may explain why BMI was a negative predictor of NAC malposition in this study (Fig. 2).

In immediate TE indwelling with NSM, the main cause of NAC malposition may be NAC adhesion at inappropriate positions on the pectoralis major muscle. In this study, immediate TE indwelling was performed in 37 cases (80.4%) and in all the TE was inserted in the submuscular pocket. In the surgery, two lamellas, skin flap and pectoral major muscle, were made, and differences in the lengths of these lamellas might have caused NAC adhesion at inappropriate positions and superior malposition. If the breast were a completely symmetrical dome in a sagittal section (Fig. 3a), with the NAC at the top, and skin contracture occurred uniformly in all direction, NAC malposition would not occur (Fig. 3b). However, actually, the breast is shaped like a tear drop, with the lower pole larger than the upper pole to a greater or lesser degree (Fig. 4a). If

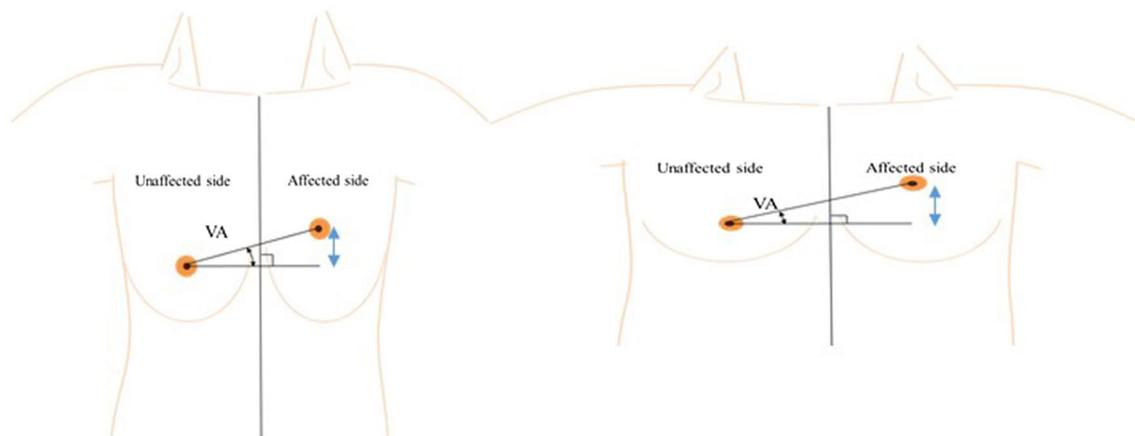


Fig. 2 A larger BMI tends to be related to a larger width of the chest wall. In patients with wide and slender chest walls, but with the same superior malposition, VA would be lower in the patient with the wider chest wall

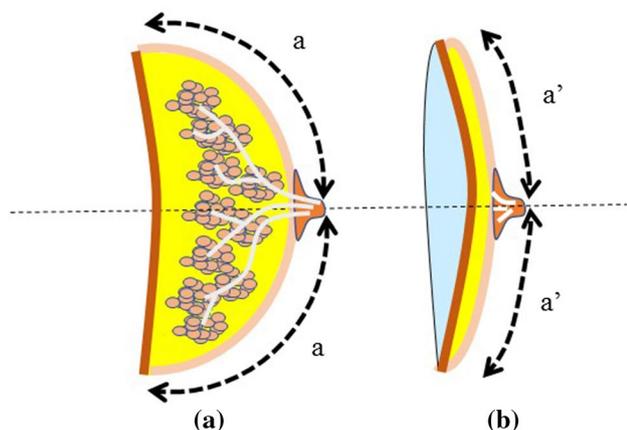


Fig. 3 If the breast were a completely symmetrical dome in a sagittal section, with the NAC at the top, and skin contracture occurred uniformly in all directions, NAC malposition would not occur

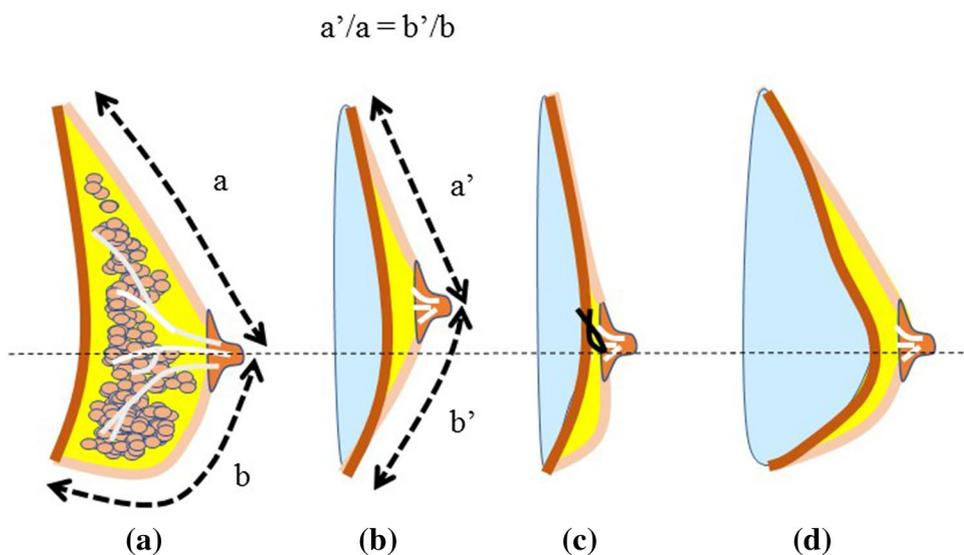
skin contracture similarly occurred uniformly in all directions, superior malposition may occur, as noted by Mori et al. [16] (Fig. 4b). A few absorbable sutures, which are placed to stitch the posterior border of the nipple on the area of the pectoralis major muscle corresponding to a position marked preoperatively, might be useful for prevention of NAC superior malposition [17] (Fig. 4c). Our study suggests that it might also be useful to fill the TE with saline to achieve the maximum possible expansion as early as possible after surgery without compromising blood supply to the mastectomy flap (Fig. 4d). However, even with use of these prevention methods, superior malposition sometimes occurred, which may be due to other causes. At full expansion of the TE, NAC tends to migrate in the upper and lateral directions (Table 1). This might

be because the composite of skin with NAC and pectoral major muscle contracts in an upper-lateral direction during expansion, due to insertion of the pectoral major muscle. This reason is speculative, but might partly account for upper malposition.

Autologous reconstruction was a positive independent predictor of HDR, although R^2 was only 0.123 ($B = 0.067$, $p = 0.027$, $\beta = -0.350$). Mori et al. reported a HDR of 0.95 after implant reconstruction, which indicates that NAC tended to migrate somewhat medially after implant reconstruction. This is a similar finding to our results (Table 3). In contrast, in autologous reconstruction, NAC tended to move a little to the lateral side of the implant. This might be because autologous breast tissue is softer than the implant and tends to droop laterally with NAC.

In conclusion, we evaluated nipple–areolar malposition after NSM and the factors associated with malposition in two-stage surgery using autologous tissue or implant reconstruction. We also evaluated how malposition after expansion of the expander with saline changed after the implant or flap replacement surgery. The total amount of saline injected into the expander and aging were significant predictors of superior malposition of NAC, both just before and more than 1 year after autologous tissue or implant insertion. The amount of saline solution injected into the expander until 2 weeks after expander insertion and BMI were significant predictors of decreased superior malposition, and autologous reconstruction was also a significant negative predictor of superior malposition at more than 1 year after the surgery. Superior NAC malposition resulting after expansion of the expander improved more after autologous reconstruction than after implant surgery.

Fig. 4 **a** The breast is shaped like a tear drop, with the lower pole larger than the upper pole to some degree. **b** If $a'/a = b'/b$, superior malposition of NAC would occur, as noted by Mori et al. [16]. **c** A few absorbable sutures were placed to stitch the posterior border of the nipple on the area of the pectoralis major muscle corresponding to a position marked preoperatively. **d** The TE was filled with saline to achieve the maximum possible expansion as early as possible after surgery without compromising blood supply to the mastectomy flap



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Compliance with ethical standards

Conflict of interest The authors have declared that no conflicts of interest exist.

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