Impact of body mass index on locoregional control in Saudi patients with breast cancer after breast conserving surgery and modified radical mastectomy

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Abstract

Background: Obesity and increased body mass index (BMI) are increasing among Saudi women across the all age groups, with an overall prevalence of 44%. Increased BMI is associated with advanced stage breast cancer and dismal survival; however, impact of BMI on locoregional control (LRC) is less studied. We aimed to evaluate the impact of BMI on LRC in Saudi patients with breast cancer after breast conserving surgery (BCS) and modified radical mastectomy (MRM).

Materials and methods: Between February 1988 and August 2008, 112 patients with breast cancer were treated with BCS and MRM followed by adjuvant chemotherapy and radiotherapy. Median age was 47.01 years (23-76). Mean BMI was 38.1 kg/m² (15.7-52.8); BMI 18.5-25 kg/m² (normal weight) in 20 (17.8%), BMI 26-30 kg/m² (overweight) in 32 (28.6%), BMI 31-40 kg/m² (obese) in 48 (42.9%) and BMI > 40 kg/m² (morbid obese) in 12 (10.7%). Median follow up period was 9 years (5-17). Cox proportional hazard analysis was done using SPSS 19.0.

Results: Total ten locoregional recurrences (8.93%) were seen. The 5 and 10 years LRC were 86.4% and 86.4% respectively. Multivariate analysis showed poor LRC in BMI 26-30 kg/m² (HR: 3.4; 95% CI.3.0-3.8, p 0.01). Other factors associated with poor LRC were; age less than 40 years, premenopausal status, and no adjuvant radiotherapy, and T4, N2 and N3 stages.

Conclusion: Overweight and obese patients had better locoregional control in our study, however, further larger trials are warranted.

Keywords: Body mass index, breast cancer, breast conserving surgery, modified radical mastectomy

Introduction

Obesity and overweight (body mass index >26 kg/m²) are increasing among both sexes and across all age groups in Kingdom of Saudi Arabia with an overall prevalence of 44% in Saudi women [1]. Obesity is known as the major factor for development of breast cancer which is the most common malignancy in Saudi Arabia; accounting for 26% of all newly diagnosed breast cancers in Saudi women and with incidence of 21.6 per 100,000 [2]. Some of studies have revealed a clear positive association between increased body mass index (BMI) and risk of developing breast cancer by 30-50% [3,4].

Elevated BMI has been shown to be associated with a poorer prognosis in breast cancer patients regardless of the menopausal status and increased mortality from other obesity-driven health problems [5], but retrospective data remained failed to show any impact of BMI on post treatment locoregional recurrence (LRR) in breast cancer patients [6-8]. Recently, results from a French trial have shown that breast cancer patients with low BMI are at high risk of LRR after breast conserving surgery (BCS) followed by adjuvant chemotherapy and radiotherapy [9]. However, no data addressing direct impact on BMI on LRR in breast cancer patients after modified radical mastectomy (MRM) is available. The purpose of this study was to evaluate the impact BMI on LRR in Saudi patients with breast cancer treated with BCS or MRM followed by adjuvant hormonal, chemotherapy and adjuvant radiotherapy.

Materials and methods

After approval from Institutional Ethical Review Board (IRB) committee, records of 112 patients with breast cancer treated between February 1988 and August 2008 with BCS and MRM followed by adjuvant chemotherapy and radiotherapy were reviewed retrospectively and comprised the study population. Inclusion criteria were; (a) histopathological confirmed breast cancer, (b) T1-T4, N0-N2, (c) underwent BCS or MRM +/- adjuvant hormonal, chemotherapy and adjuvant radiotherapy. Exclusion criteria were; (a) presence of distant metastasis, (b) neoadjuvant chemotherapy and (c) inflammatory or inoperable tumors.

BMI calculation

Each patient was categorized according to BMI. Height and weight were measured at the time of surgery using institutional
protocols and BMI was calculated using the formula of weight in kilograms divided by the square of the height in meters (kg/m²). BMI was then categorized into five groups as follows: underweight as BMI <18.5 kg/m²; normal weight as BMI from 18.5 to 25 kg/m²; overweight as BMI from 25 to 30 kg/m²; obese as BMI from 31 to 40 kg/m²; and morbid obese as BMI above 40 kg/m².

Clinical and histologic variables likely to influence the risk of LRR were studied as:

**Clinical variables**

Age, menopausal status, associated comorbidities, BMI groups, initial tumor size on physical, mammography and sonography examination, laterality and location of primary tumor. Surgery was performed either wide local excision or MRM with axillary lymph node dissection.

Adjuvant chemotherapy or hormonal therapy was given 4-5 weeks after surgery followed by radiotherapy.

**Histopathological variables**

Histopathological types of tumors according to WHO 1981 classification of breast tumors, grade according to Scarff Bloom and Richardson classification, pathological size of tumor, presence/absence of estrogen receptors (ER), progesterone receptors (PR), Her 2 neu overexpression, number of retrieved axillary lymph nodes and number of positive nodes, nodal density, presence of lymphovascular space invasion (LVSI) and margin status (negative or positive).

**Statistical analysis**

The primary endpoints were LRR and locoregional control (LRC). Secondary endpoints were disease free survival (DFS) and overall survival (OS). The times to last follow up evaluation, appearance of local relapse and death were calculated from date of starting treatment. LRR was defined as any recurrence of tumor within the treated breast, chest wall or ipsilateral axilla and overlying skin. Skin recurrence was considered as local failure when located exclusively in ipsilateral breast or chest wall. Local recurrences occurring synchronously with distant metastasis were also included. DFS was defined as the duration between the entry date and the date of documented disease reappearance, death from cancer and/or last follow-up (censored). OS was defined as the duration between the entry date and the date of patient death or last follow-up (censored). Probabilities of LRC and DMC, DFS and OS were determined with the Kaplan-Meier method. The comparisons for various endpoints were performed using log rank test and Cox regression analysis. Univariate and multivariate analyses were also performed for different prognostic factors for LRR. All statistical analyses were performed using the computer program SPSS version 16.0.

**Results**

Median follow up period was 9 years (range: 5-17). Patients’ characteristics according to BMI subgroups are shown in (Table 1).

**Clinical characteristics**

Mean age of cohort was 47.0 years (range: 23-76; standard deviation (SD) 10.3. According to menopausal status, 93 patients (83.0%) were premenopausal and 19 patients (17.0%) were postmenopausal. Mean BMI was 31.8 kg/m² (range: 15.7-52.8; SD7.2). According to comorbidities, 72 patients (64.3%) had no comorbidities. Common morbidities in 40 patients (35.7%) were: hypertension in 14 patients (12.5%), diabetes in 9 patients (8.0%) and combined hypertension and diabetes in 6 patients (5.4%). Family history was positive in 17 patients (15.2%). In four patients (3.6%) there was bilateral breast cancer at the time of diagnosis. Majority of cohort (57 patients; 79.6%) had left side breast cancer and outer lower quadrant was common site of tumor location (50 patients; 45.9%) followed upper outer quadrant (30 patients; 27.5%). Mean mammography size of tumor was 3.9 cm (range: 1-7; SD 2.3). Mean baseline CA15.3 level was 31.1 units/ml (range: 1-94.3; SD 23.9).

**Histopathological characteristics**

Mean pathological tumor size was 3.4 cm (range: 1-10; SD 2.4) and infiltrating ductal carcinoma (IDC) was predominant histopathological variant seen in 95 patients (88.0%). Majority of tumors were moderately differentiated of grade 2 (68 patients; 60.7%). According to marginal status, 77 patients (68.8%) had negative margins. Majority of cohort was ER and PR positive (65 patients; 58.0%) and Her 2 neu overexpression was seen in 10 patients (8.9%).

**Treatment characteristics**

Majority of patients had MRM (77 patients; 71.3%) followed by BCS in 31 patients (28.7%). Mean axillary retrieved lymph nodes were 14.1 (2-42) after axillary dissection and sentinel node dissection.

Total 70 patients (62.5%) received adjuvant chemotherapy which was given within 5-6 weeks (range: 3-11) of surgery. Adjuvant chemotherapy protocols were as; CMF (18.6%), AC (20.6%), AC followed Paclitaxal (32.9%), FAC (32.9%), TAC (5.9%), AT (5.7%), FAC-TAC (4%).

Total 89 patients (83.0%) received local radiation therapy which was started 22 weeks (18-26) after the surgery and 3-5 weeks after the completion of chemotherapy. For BCS patients, whole breast radiation therapy was delivered in 2 Gy fractions to mean total mean dose of 50 Gy (45-64) and for MRM patients, chest wall radiation therapy was given in 2 Gy fractions to mean total dose 50 Gy (50-60). For positive axillary nodes, supra-clavicular fields were used and given mean total dose of 45 Gy (42.5-50). All patients were treated using three dimensional conformal radiation therapy (3DCRT) and on multileaf collimator (MLC) assisted linear accelerator. Hormonal therapy was given to 66 patients (8.9%) in form of tamoxifen (46.4%), letrozole (9.8%) and sequential regimen
Table 1. Patients characteristics according to body mass index groups.

| Variables                        | 18.6-25 Kg/m² | 26-30 Kg/m² | 31-40 Kg/m² | > 40 Kg/m² |
|----------------------------------|---------------|-------------|-------------|-----------|
| Number                           | 20 (17.8%)    | 32 (28.6%)  | 48 (42.9%)  | 12 (10.7%)|
| Age (years) mean                 | 38.2          | 44.9        | 47.0        | 54.7      |
| Gender                           |               |             |             |           |
| Female                           | 19 (16.9%)    | 31 (27.7%)  | 48 (42.9%)  | 12 (10.7%)|
| Male                             | 1 (0.9%)      | 1 (0.9%)    | -           | -         |
| Menopausal status                |               |             |             |           |
| Premenopausal                    | 18 (16.1%)    | 28 (25.0%)  | 37 (33.1%)  | 10 (8.9%) |
| Postmenopausal                   | 2 (1.8%)      | 4 (3.6%)    | 11 (9.8%)   | 2 (1.8%)  |
| Co morbidities                   |               |             |             |           |
| DM                               | -             | 1 (0.9%)    | 6 (5.4%)    | 2 (1.8%)  |
| HTN                              | 2 (1.8%)      | 3 (2.7%)    | 8 (7.2%)    | 1 (0.9%)  |
| HL                               | 1 (0.9%)      | -           | 1 (0.9%)    | -         |
| DM + HTN                         | -             | 3 (2.7%)    | 2 (1.8%)    | 1 (0.9%)  |
| HL + DM + HTN                    | -             | 4 (3.6%)    | 4 (3.6%)    | 1 (0.9%)  |
| Medication for DM                |               |             |             |           |
| Insulin                          | -             | -           | 1 (0.9%)    | -         |
| Sulfonylureas                    | -             | -           | 2 (1.8%)    | 1 (0.9%)  |
| Metformin                        | -             | 1 (0.9%)    | 2 (1.8%)    | 1 (0.9%)  |
| Combined                         | -             | -           | 1 (0.9%)    | -         |
| Laterality                       |               |             |             |           |
| Unilateral                       | 18 (25.0%)    | 31 (27.7%)  | 47 (42.0%)  | 12 (10.7%)|
| Bilateral                        | 2 (1.8%)      | 1 (0.9%)    | 1 (0.9%)    | -         |
| Side                             |               |             |             |           |
| Right                            | 6 (5.4%)      | 4 (3.6%)    | 11 (9.8%)   | 1 (0.9%)  |
| Left                             | 12 (10.7%)    | 27 (24.1%)  | 36 (32.1%)  | 11 (9.8%) |
| T Stage                          |               |             |             |           |
| T1                               | 6 (5.4%)      | 13 (11.6%)  | 13 (11.6%)  | 3 (2.7%)  |
| T2                               | 8 (7.2%)      | 10 (8.9%)   | 22 (19.6%)  | 6 (5.4%)  |
| T3                               | 5 (4.5%)      | 4 (3.6%)    | 8 (7.2%)    | 3 (2.7%)  |
| T4                               | 1 (0.9%)      | 5 (4.5%)    | 3 (2.7%)    | -         |
| N stage                          |               |             |             |           |
| N0                               | 8 (7.2%)      | 15 (10.7%)  | 20 (20.7%)  | 7 (6.3%)  |
| N1                               | 4 (3.6%)      | 8 (7.2%)    | 21 (18.7%)  | 3 (2.7%)  |
| N2                               | 6 (5.4%)      | 4 (3.6%)    | 4 (3.6%)    | -         |
| N3                               | 2 (1.8%)      | 5 (4.5%)    | 3 (2.7%)    | 2 (1.8%)  |
| Histological type                |               |             |             |           |
| IDC                              | 15 (13.0%)    | 29 (25.9%)  | 40 (35.7%)  | 11 (9.8%) |
| ILC                              | -             | 1 (0.9%)    | 2 (1.8%)    | 1 (0.9%)  |
| IDC + ILC                        | 2 (1.8%)      | 1 (0.9%)    | 2 (1.8%)    | -         |
| Others                           | 3 (2.7%)      | 1 (0.9%)    | 4 (3.6%)    | -         |
| LVSI                             |               |             |             |           |
| Positive                         | 9 (8.1%)      | 12 (10.7%)  | 11 (9.8%)   | 3 (2.7%)  |
| Negative                         | 11 (9.8%)     | 20 (17.9%)  | 37 (33.1%)  | 9 (8.1%)  |
| Receptor status                  |               |             |             |           |
| Triple (-)                       | 1 (0.9%)      | 7 (6.3%)    | 2 (1.8%)    | 1 (0.9%)  |
| ER+                              | 2 (1.8%)      | 5 (4.5%)    | 5 (4.5%)    | 3 (2.7%)  |
| PR+                              | -             | 3 (2.7%)    | 5 (4.5%)    | 2 (1.8%)  |
| ER+/PR+                          | 4 (3.6%)      | 2 (1.8%)    | 5 (4.5%)    | -         |
| Her 2 neu+                       | 5 (4.5%)      | 8 (7.2%)    | 20 (17.9%)  | 3 (2.7%)  |
| ER+/Her 2 neu+                   | 2 (1.8%)      | 2 (1.8%)    | 2 (1.8%)    | 1 (0.9%)  |
| PR+/Her 2 neu+                   | 1 (0.9%)      | -           | 1 (0.9%)    | 1 (0.9%)  |
| Triple (+)                       | 5 (4.5%)      | 5 (4.5%)    | 8 (7.2%)    | 1 (0.9%)  |
Continuation of Table 1.

| Variables | 18.6-25 Kg/m^2 | 26-30 Kg/m^2 | 31-40 Kg/m^2 | > 40 Kg/m^2 |
|-----------|---------------|--------------|--------------|-------------|
| **Type of surgery** | | | | |
| BCS | 9 (8.1%) | 27 (24.1%) | 15 (13.4%) | 3 (2.7%) |
| MRM | 8 (7.2%) | 5 (4.5%) | 32 (28.6%) | 9 (8.1%) |

| **Chemotherapy** | | | | |
| Yes | 19 (16.9%) | 30 (26.8%) | 47 (42.0%) | 8 (7.2%) |
| No | 1 (0.9%) | 2 (1.8%) | 1 (0.9%) | 4 (3.6%) |

| **Radiation therapy** | | | | |
| Yes | 19 (16.9%) | 24 (21.4%) | 38 (34.0%) | 8 (7.2%) |
| No | 1 (0.9%) | 8 (7.2%) | 10 (8.9%) | 4 (3.6%) |

| **Hormonal therapy** | | | | |
| Yes | 14 (12.0%) | 18 (16.0%) | 25 (22.3%) | 9 (8.1%) |
| No | 6 (5.4%) | 14 (12.1%) | 23 (20.5%) | 3 (2.7%) |

in 9.8%. Mean duration of hormonal therapy was 5.5 years (range; 3.5-7.2).

**Locoregional recurrence and locoregional control**

Total ten locoregional recurrences (8.93%) were seen among 112 breast cancer patients. Four (40%) LRR occurred at scar site and 6 LRR (60%) were seen in ipsilateral axilla and supraclavicular regions. Median time of LRR was 3.6 years (range: 2.73-5.1). The actual LRC rates at 10 years were 86.4% (Figure 1). Actual 10 year distant control (DC) and overall survival (OS) rates were 74.2% (95% CI: 63.3-89.2) and 77.4% (95% CI: 66.4-82.9) respectively.

Univariate analysis of clinical prognostic factors for LRR in our cohort showed four prognostic factors influencing the LRR; (a) age less than 40 years (HR: 4.3, 95% CI: 2.8-5.1), (b) premenopausal status (HR: 3.4, 95% CI: 2.7-4.2), (c) BMI 26-30 kg/m^2 (HR: 3.4; 95% CI: 3.0-3.8) and (d) no adjuvant radiotherapy (HR: 5.2, 95% CI: 4.11-6.4) (Table 2).

Univariate analysis of histopathological prognostic factors for LRR in our cohort showed five prognostic factors influencing the LRR; (a) IDC histological type (HR: 2.2, 95% CI: 1.6-3.0), (b) stage T4 (HR: 1.8, 95% CI: 1.2-2.2), (c) N2 and N3 nodal status (HR: 1.8, 95% CI: 2.1-4.0), (d) negative ER status (HR: 1.2, 95% CI: 1.1-1.5) and (e) Her 2neu overexpression (HR: 2.1, 95% CI: 1.7-2.7) (Table 3).

In multivariate analysis, age less than 35 years, BMI 26-30 kg/m^2, premenopausal status, no adjuvant radiotherapy, T and N stage were still independent important prognostic factors for LRR in our cohort (Table 4).

According to BMI groups, patients with BMI above 31 kg/m^2 had better LRR in comparison to normal and underweight patients (Figure 2).

**Discussion**

Breast cancer is the major public health concern in Saudi Arabia as it is the commonest cancer among women with overall percentage of 22.4. The most common age group found to be affected is 20-45 years with age-specific incidence of breast cancer is 45 per 100,000 at the age of 45 years [10]. Obesity is known as causative factor for the development of breast cancer and is associated with dismal prognosis in breast cancer patients because of delayed diagnosis among overweight women or the growth and spread of breast cancer may be more rapid in obese women and consequently, obese women would tend to have more recurrences [11]. In Saudi Arabia 80% of premenopausal women are either overweight or obese which alarms the grave prognosis of breast cancer as compared to other parts of the world [12]. However impact of obesity or increased BMI on locoregional control in breast cancer is not clear.
cancer patients has not been studied. Our retrospective data showed two interesting relationships; (a) an inverse association between BMI and LRR and (b) positive relationship between BMI (26-30 kg/m²) and LRR. The risk of LRR markedly reduced in obese (BMI above 31 kg/m²) and morbid obese patients. This could be explained by three hypotheses:

1) Bad clinical and histopathological features in patients with BMI of 18.6-30 kg/m² in our cohort. Thin premenopausal women tend to have more high levels of endogenous estrogen level than obese premenopausal women, which enhances the risk LRR [13].

2) Patients below 30 kg/m² had high breast conserving surgery. The relationship between tumor size and breast volume might be another explanation. Women with lower BMI have smaller breast and less adipose tissue which makes difficult for wide negative margins during lumpectomy [14].

3) In our cohort obese and morbid obese patients had more

Table 2. Univariate analysis of clinical prognostic factors for locoregional recurrence in breast cancer patients.

| Prognostic factor | Hazard ratio | 95% CI | p-value |
|-------------------|--------------|--------|---------|
| Age groups (years) |              |        |         |
| Below 25          | 6.2          | 4.2-7.3| 0.001   |
| 25-35             | 3.7          | 2.6-4.1| 0.002   |
| 36-40             | 3.1          | 1.7-3.9| 0.004   |
| Above 40          | 1.0          | -      | -       |

| Menopausal status | |        |
|-------------------|--------|--------|
| Premenopausal     | 3.8    | 2.7-4.2| 0.002 |
| Postmenopausal    | 0.8    | 0.2-0.9| 0.001 |

| BMI (Kg/m²)       | |        |
|-------------------|--------|--------|
| 18.5-25           | 1.0    | -      | -      |
| 26-30             | 3.3    | 2.6-4.8| 0.002 |
| 31-40             | 0.9    | 0.5-1.0| -      |
| Above 40          | 1.0    | -      | -      |

| Type of surgery   | |        |
|-------------------|--------|--------|
| BCS               | 1.1    | 0.8-1.6| 0.9    |
| MRM               | 1.1    | 0.8-1.6| 0.9    |

| Chemotherapy      | |        |
|-------------------|--------|--------|
| Yes               | 0.7    | 0.4-1.1| 0.2    |
| No                | 1.1    | 0.8-1.6| 0.9    |

| Adjuvant radiotherapy | |        |
|-----------------------|--------|--------|
| Yes                   | 0.4    | 0.3-0.8| 0.001 |
| No                    | 5.2    | 4.11-6.4| 0.001 |

| Hormonal therapy    | |        |
|---------------------|--------|--------|
| Yes                 | 1.0    | 0.8-1.6| 0.2    |
| No                  | 1.1    | -      |        |

Table 3. Univariate analysis of histopathological prognostic factors for locoregional recurrence in breast cancer.

| Prognostic factor | Hazard ratio | 95% CI | p-value |
|-------------------|--------------|--------|---------|
| Histologic type   |              |        |         |
| IDC               | 2.2          | 1.6-3.0| 0.03    |
| ILC               | 1.3          | 1.1-1.6| 0.4     |
| IDC+ILC           | 3.1          | 1.7-3.9| 0.002   |
| others            | 1.0          | -      | -       |

| T stage | |        |
|---------|--------|--------|
| T1      | 0.8    | 0.5-1.0| 0.2    |
| T2      | 1.0    | 0.7-1.3| 0.2    |
| T3      | 1.3    | 1.1-1.6| 0.9    |
| T4      | 1.8    | 1.2-2.2| 0.02   |

| N stage | |        |
|---------|--------|--------|
| N0      | 1.1    | 0.8-1.6| 0.002 |
| N1      | 1.1    | 0.8-1.6| -      |
| N2      | 1.3    | 2.6-4.8| 0.002 |
| N3      | 2.4    | 1.7-3.2| 0.001 |

| LVSI | |        |
|------|--------|--------|
| Present | 1.7| 0.8-1.9| 0.3 |
| Absent | 1.1| 0.8-1.6| - |

| Margins | |        |
|---------|--------|--------|
| Negative | 0.7| 0.4-1.1| 0.2 |
| Close or positive | 1.1| 0.8-1.6| 0.9 |

| Estrogen receptors | |        |
|--------------------|--------|--------|
| Positive | 0.4| 0.3-0.8| 0.001 |
| Negative | 1.2| 1.1-1.5| 0.06 |

| Progesterone receptors | |        |
|------------------------|--------|--------|
| Positive | 0.6| 0.5-0.9| 0.01 |
| Negative | 1.1| 0.8-1.6| - |

| Her 2 neu expression | |        |
|----------------------|--------|--------|
| Yes | 2.1| 1.7-2.7| 0.002 |
| No | 1.1| 0.8-1.6| - |

ER and PR receptors and use of hormonal therapy is associated with low risk of LRR as compared to overweight patients [15].

Strengths of our study were long follow up period, availability of complete data and adjustment of other confounding factors (co-morbidities, TNM staging) factors before multivariate analysis; however our study can be criticized for (a) low sample size, (b) we did not looked into impact of BMI on distant failure which shall be addressed in large prospective trials, (c) no data on waist size measurements and life style (dietary habits and exercise) was collected and (d) we did not see the impact post-treatment BMI on local control outcome.

Conclusion
Breast cancer patients with BMI >31 Kg/m² had better locoregional control recurrences as compared to other BMI
Table 4. Multivariate analysis of prognostic factors for locoregional recurrence in breast cancer.

| Prognostic factor          | Hazard ratio | 95% CI   | p-value |
|----------------------------|--------------|----------|---------|
| **Age groups (years)**     |              |          |         |
| Below 25                   | 3.4          | 2.9-3.9  | 0.01    |
| 25-35                      | 2.7          | 2.2-3.1  | 0.02    |
| 36-40                      | 2.1          | 1.5-2.6  | 0.04    |
| Above 40                   | 1.0          | -        | -       |
| **Menopausal status**      |              |          |         |
| Premenopausal              | 2.4          | 1.9-2.9  | 0.03    |
| Postmenopausal             | 1.0          | -        | -       |
| **BMI (Kg/m²)**            |              |          |         |
| 18.5-25                    | 1.0          | -        | -       |
| 26-30                      | 3.4          | 3.0-3.8  | 0.01    |
| 31-40                      | 1.0          | -        | -       |
| Above 40                   | 1.0          | -        | -       |
| **Adjuvant radiotherapy**  |              |          |         |
| Yes                        | 0.8          | 0.6-1.0  | 0.04    |
| No                         | 3.8          | 3.4-4.2  | 0.002   |
| **T stage**                |              |          |         |
| T3                         | 1.2          | 0.8-1.4  | 0.05    |
| T4                         | 1.8          | 1.3-2.2  | 0.04    |
| **N stage**                |              |          |         |
| N2                         | 1.2          | 0.9-1.5  | 0.05    |
| N3                         | 1.9          | 1.4-2.3  | 0.04    |

CI= confidence interval, BMI= body mass index, T= primary tumor size, N= axillary nodal status

Authors’ contributions

| Authors’ contributions | EFA | ARJAG | MAT | YB |
|------------------------|-----|-------|-----|----|
| Research concept and design | ✓   | --    | --  | -- |
| Collection and/or assembly of data | --  | ✓     | --  | ✓  |
| Data analysis and interpretation | --  | --    | ✓   | -- |
| Writing the article | ✓   | --    | --  | ✓  |
| Critical revision of the article | ✓   | --    | --  | ✓  |
| Final approval of article | ✓   | ✓     | ✓   | ✓  |
| Statistical analysis | --  | --    | --  | ✓  |

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Figure 2. Cumulative locoregional control in cohort according to BMI subgroups.

The authors declare that they have no competing interests.

groups, however further larger trials are warranted to answer this question.

Competing interests
The authors declare that they have no competing interests.
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