

# Comparative Study of Single Axillary Drain Versus Combined Axillary and Pectoral Drain in Prevention of Seroma After Modified Radical Mastectomy

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## ABSTRACT

**Background:** Modified radical mastectomy (MRM) is still one of the most commonly used surgical techniques for breast cancer and in some selected patient it's the only surgery to be performed. seroma is one of the most frequent complication which is usually formed under skin flaps or in the axilla as reported as much as 30% in some studies. The use of closed suction drainage system reduce the incidence of seroma formation and has been accepted by most of surgeons; however, the time at which the drain should be removed and the number of drains inserted in the wound are still controversial.

**Aim:** The present study compares the results of single axillary versus axillary and pectoral drain insertion in patients undergoing MRM for breast cancer.

**Materials and Methods:** The present study was conducted on 60 female patients with stage I and stage II breast cancer who were candidate for modified radical mastectomy (MRM) admitted to the Surgical Oncology Unit, Alexandria Main University Hospital. Patients were randomly classified into two equal groups, 30 patients each.

**Result:** Patients were randomly classified into two equal groups. Group (A) had modified radical mastectomy (MRM) with axillary and pectoral drains, Group (B) had modified radical mastectomy (MRM) with single axillary drain, there was no significant difference between the two groups in terms of Age (P=0.940), BMI (P=0.719), Size of breast (0.893), Site of lesion (0.943), Neoadjuvant treatment (P=0.297), Size of mass (P=1.000), Contraceptive pills (P=0.301), duration of operation (P=0.218), Intra operative blood loss (P=0.331), methods of axillary dissection (P=0.795), Numbers of LN removed (P=0.334), Total amount collected (P=0.114), Day of drain removed (P=0.106) and seroma formation (P=0.417). A statistical significance between two groups were found in term of total amount per day (P=0.025), hematoma formation (P=0.024)

**Conclusion:** This study revealed that one drain insertion after modified radical mastectomy (MRM) surgery is as effective as two drains, however some patients experience less seroma formation and early drain removal using single axillary drain without seroma formation. Also it was found that single axillary drain is suitable certain type of people which could have a benefit using single axillary drain

**Keywords:** MRM, modified radical mastectomy, drain, seroma.

## INTRODUCTION

Breast Cancer constitutes a major public health issue globally with over 1 million new cases diagnosed annually, resulting in over 400,000 annual deaths and about 4.4 million women living with the disease. It is the commonest site specific malignancy affecting women and the most common cause of cancer mortality in women worldwide. <sup>(1,2)</sup>

Variable operations and techniques have been used to treat breast cancer but modified radical mastectomy is still the most common operation used. <sup>(3)</sup>

There are a lot of complication that could develop after modified radical mastectomy but seroma is the most

common complication that develop after this type of operation with an incidence of 3 to 85 %. <sup>(4)</sup>

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Seroma impair the healing of the wound; that is why drains are usually left in place for 1-3 weeks, until the skin flaps heal and adhere to chest wall, as evidenced by diminished drain output.<sup>(5)</sup>

Various methods techniques have been used to reduce the incidence of seroma formation which include shoulder immobilization,<sup>(6)</sup> perioperative use of tranexamic acid,<sup>(7)</sup> prolonged suction drainage,<sup>(8)</sup> and flap fixation.<sup>(9, 10)</sup>

Seroma formation is most likely the result of inflammatory response due to wound healing; several factors have been detected in seroma fluids that support this assumption. These factors are high level of IgG, leukocytes, granulocytes, proteinase inhibitors and different kinds of cytokines (tPA, uPAR, PAI-1, PAI-2, IL-6, IL1) And inhibition of the inflammatory response might result in a decrease in seroma formation, and perhaps improve the quality of life after mastectomy.<sup>(11, 12)</sup>

Both age and hypertension are considered to be risk factors for seroma formation. Those Patients older than 45 with hypertension have a greater risk of developing seroma than those younger patients without hypertension.<sup>(13)</sup>

Unlike hematomas and lymphoceles, seromas form from a translocation of fluid without a structural channel (vascular or lymphatic). Therefore, drains can prevent the development of a significant seroma as they are not obligated to close channels. By controlled drainage of a seroma, the dead space can be limited, allowing time for the inflammatory gradient to subside.<sup>(14)</sup>

Drains may be classified as open or closed system, and active or passive depending on their situation or function.<sup>(15)</sup> Use of drains has been a common surgical practice to obliterate the dead space created during surgery. Drains is used both prophylactically and therapeutically.<sup>(16)</sup>

Patients can be safely discharged with drains in situ with adequate patient education and coordination of inpatient and outpatient facilities, including telephone contacts.<sup>(16)</sup>

Concerns expressed in the early discharge group of patients include personal care, bed posture, dressing themselves, fatigue, loneliness, pain, and worries about the wound and the arm. Despite these factors, studies have shown that patient acceptance of early discharge with drains in situ remains good.<sup>(16)</sup>

It is common practice to remove drains when drainage decreases to a minimal volume (20-50 mL) in the preceding 24 hours to minimize seroma formation. It has been shown that 48 hours after surgery, as much as 74% of the total volume of seroma has been drained.<sup>(16)</sup>

## METHODS

The present study were conducted on 60 female patients with breast cancer admitted to the Surgical Oncology Unit, Alexandria Main University Hospital during 2016-2017. Patients were submitted to modified radical mastectomy (MRM). Patients were randomly classified into two equal groups, 30 patients each as group (A) had modified radical mastectomy (MRM) with axillary and pectoral drains and group (B) had modified radical mastectomy (MRM) with single axillary drain.

Those patients had their breast cancer between stage I and stage II proved by history taking, examination, imaging studies (mammogram and/ or MRI) and biopsy (FNAC or tru-cut biopsy). Metastasis was excluded by metastatic work up in the form of US abdomen, CT chest, and bone scan if needed.

### Exclusion Criteria:

Patients with distant metastases, synchronous or meta-chronous contralateral breast cancers, History of chest wall irradiation.

Patients who received neoadjuvant chemotherapy as a result of having locally advanced breast cancer were included in the study.

All the patients had routine laboratory investigations including: Complete blood picture. Bleeding and coagulation profile, fasting blood sugar. Renal function tests (blood urea nitrogen and creatinine) Liver function tests (ALT, AST, serum albumin, serum bilirubin) if needed.

The patients were divided into two separate groups randomly. All patients underwent general anesthesia and MRM surgery was performed .After surgery, removed breast masses were weighed, and sent for pathologic evaluation and the results were recorded in TNM staging system. After surgery, patients were followed up for one month.

Patients were discharged with drains after 48 hours, depending on general health condition (fever, nausea, vomiting, wound complications, normal physical activity). Patients were trained how to empty the drains, and measure and record the volume of the fluid and were advised to return to hospital for removing drains when their discharge were below 30 cc per day or on the 10th post-operative.

After removing the last drain all patients were checked weekly for one month, and if any seroma formation is detected it were aspirated and the wound were dressing with compressive bandage.

In the setting of seroma formation, wounds were checked every other day to determine re-accumulation of seroma. Aspiration were continue until no further seroma is observed. Timing of seroma formation and volume of aspirated fluid were recorded.

We compared between the two groups as regard to, total operative time, Intra operative blood loss (weight of post-operative soaked towels to pre-operative dry ones), Total amount of fluid that emerged via the drain, amount of fluid that emerged via the drain from the first post-operative day till drain removal, duration till removal of the drain, Post-operative complications such as wound infection, seroma formation, hematoma, etc.

## RESULTS

In our study we found no statistical significance between group A and group B in terms of age, BMI, (Table-1). Similarly no statistical significance between two groups were found in term of neoadjuvant treatment, size of breast, site of lesion, size of mass, chronic medical disease, contraceptive pills (Table-2), duration of operation, intra operative blood loss, methods of axillary, numbers of LN removed (Table-3), total amount collected,

day of drain removed , Seroma formation (Table-4). However a statistical significance between two groups were found in term of Total amount per day (P=0.025) and Hematoma formation (P=0.024) (Table-4).

**Table-1. Comparison between the two studied groups according to demographic data**

| demographic data         |      | Group A (two drains)<br>N = 30 | Group B (one drain)<br>N=30 | P value |
|--------------------------|------|--------------------------------|-----------------------------|---------|
| AGE                      | Mean | 53.63 ± 9.37                   | 53.83 ± 11.0                | 0.940   |
| BMI (kg/m <sup>2</sup> ) | Mean | 30.06 ± 4.14                   | 29.62 ± 5.17                | 0.719   |

A comparison between seroma formation with group A and B were done and we found that in group A their was a statistical significance between those who developed seroma and those who did not in term of duration of operation, Total amount collected, Total amount per day, intra operative blood loss, methods of axillary dissection (Table-5) similarly in group B a statistical significance were found between those who developed seroma and those who did not it term of BMI (kg/m<sup>2</sup>), Total amount collected ,Total amount per day , methods of axillary dissection (Table-6).

## DISCUSSION

In our study regarding the age most of our patients in group A ranged from 51 to 60 years and also for group B most of patients ranged from 51 to 60 years. no statistical

significance between two groups

Relatively few reports on the effect of patient age on seroma formation in women undergoing MRM have been published so far. (17,18) in other publications no correlation between patient age and seroma formation incidence were noted. (19,13)

Variable explanations has shown a relation between sarcoma formation with different causative factors. (13) As intraoperative blood loos methods of axillary dissection and longer operation time (20, 21)

In our study a statistical significance was found in comparison between body mass index and seroma formation in patients with single axillary drain, most of those patients who developed seroma were morbidly obese.

Higher incidence of seroma was noted in obese patients who were in accordance with series of Burak et al. (22) and van Bommel et al. (23) this can be explained on the basis of increased serous exudation in tissues with higher content of adipose cells, and associated co-morbidities commonly found in obese however Gonzalez et al. Did not observe an effect of obesity on seroma formation. (17)

In a study done by Porter et al. (24) reported that the use of electrocautery in mastectomy reduces blood loss but increased the rate of seroma formation and it was the same comparing to our study especially in axillary dissection we found that patients in Group A those who developed seroma had their axillary dissection using diathermy and those who did not developed serom had axillary dissection using scissors.

The same was noticed in group B those who developed seroma had their axillary dissection using diathermy. While for those who did not, most of them had

**Table-2. Comparison between the two studied groups according to clinical parameters**

| Clinical Parameters     |         | Group A (two drains)<br>N = 30 | Group B (one drain)<br>N=30 | P value |
|-------------------------|---------|--------------------------------|-----------------------------|---------|
| Neoadjuvant             | No. (%) | 15 (50.0%)                     | 11 (36.7%)                  | 0.297   |
| Size of breast          |         |                                |                             |         |
| A                       |         | 1 (3.3%)                       | 1 (3.3%)                    |         |
| B                       |         | 12 (40.0%)                     | 13 (43.3%)                  |         |
| C                       | No. (%) | 17 (56.7%)                     | 15 (50.0%)                  | 0.893   |
| D                       |         | 0 (0.0%)                       | 1 (3.3%)                    |         |
| Site of lesion          |         |                                |                             |         |
| Retroareolar            |         | 8 (26.7%)                      | 10 (33.3%)                  |         |
| Upper inner             |         | 7 (23.3%)                      | 7 (23.3%)                   |         |
| Upper outer             | No. (%) | 13 (43.3%)                     | 13 (43.3 %)                 | 0.943   |
| Lower inner             |         | 1 ( 3.3 %)                     | 0 (0.0%)                    |         |
| Inner outer             |         | 1 ( 3.3 %)                     | 0 (0.0%)                    |         |
| Size of mass            |         |                                |                             |         |
| <2                      |         | 1 (3.3%)                       | 1 (11.1%)                   |         |
| 2 – <5                  | No. (%) | 22 (73.3%)                     | 7 (77.8 %)                  | 1.000   |
| ≥5                      |         | 7 (23.3%)                      | 1 (11.1%)                   |         |
| Chronic medical disease | No. (%) | 15 (50.0%)                     | 17 (56.7%)                  | 0.605   |
| Contraceptive pills     | No. (%) | 18 (60.0%)                     | 14(46.7%)                   | 0.301   |

**Table-3. Relation between the two studied groups according to operative parameters**

| operative parameters                  |         | Group A (two drains)<br>N = 30 | Group B (one drain )<br>N=30 | P value |
|---------------------------------------|---------|--------------------------------|------------------------------|---------|
| <b>Duration of operation</b>          | Mean    | 1.66 ± 0.38                    | 1.80 ± 0.38                  | 0.218   |
| <b>Intra operative blood loss</b>     |         |                                |                              |         |
| 200>                                  | No. (%) | 15 (50.0%)                     | 10 (33.3%)                   | 0.331   |
| 300-200                               |         | 13 (43.3%)                     | 15 (50.0%)                   |         |
| 300<                                  |         | 2 (6.7 %)                      | 5 (16.7%)                    |         |
| <b>Methods of axillary dissection</b> |         |                                |                              |         |
| Dissection by scissors                | No. (%) | 14 (46.7%)                     | 13 (43.3%)                   | 0.795   |
| Dissection by diathermy               |         | 16 (53.3%)                     | 17 (56.7%)                   |         |
| <b>Numbers of LN removed</b>          | Mean    | 12.10 ± 3.06                   | 12.73 ± 2.78                 | 0.334   |

**Table-4. Comparison between the two studied groups according to postoperative diameter**

| Postoperative Diameter        |         | Group A (two drains)<br>N = 30 | Group B (one drain)<br>N=30 | P value |
|-------------------------------|---------|--------------------------------|-----------------------------|---------|
| <b>Total Amount Collected</b> | Mean    | 1600.67 ± 319.32               | 1417.17 ± 421.93            | 0.114   |
| <b>Total Amount Per Day</b>   | Mean    | 137.58 ± 24.16                 | 120.64 ± 22.97              | 0.025*  |
| <b>Day of drain removed</b>   |         |                                |                             |         |
| 8th                           | No. (%) | 0 (0.0%)                       | 2 (6.7%)                    | 0.114   |
| 9th                           |         | 3 (10.0%)                      | 5 (16.7%)                   |         |
| 10th                          |         | 3 (10.0%)                      | 3 (10.0%)                   |         |
| 11th                          |         | 8 (26.7%)                      | 1 (3.3%)                    |         |
| 12th                          |         | 7 (23.3%)                      | 8 (26.7%)                   |         |
| 13th                          |         | 7 (23.3%)                      | 5 (16.7%)                   |         |
| 14th                          |         | 2 (6.7%)                       | 6 (20.0%)                   |         |
| <b>Haematoma</b>              | No. (%) | 0 (0.0%)                       | 6 (20%)                     | 0.024*  |
| <b>Seroma</b>                 | No. (%) | 12 (40.0%)                     | 9 (30%)                     | 0.417   |

**Table-5. Significant Uivariant analysis regarding seroma formation in group A**

|                                       |         | Non seroma<br>Mean ± SD<br>(n = 18) | Seroma<br>Mean ± SD<br>(n = 12) | P value |
|---------------------------------------|---------|-------------------------------------|---------------------------------|---------|
| <b>Duration of Operation</b>          | Mean    | 1.54 ± 0.33                         | 1.85 ± 0.38                     | 0.023*  |
| <b>Total Amount Collected</b>         | Mean    | 1418.56 ± 156.71                    | 1873.83 ± 308.52                | <0.001* |
| <b>Total Amount Per Day</b>           | Mean    | 128.01 ± 16.62                      | 151.92 ± 27.15                  | 0.011*  |
| <b>Intra operative blood loss</b>     |         |                                     |                                 |         |
| < 200                                 | No. (%) | 14 (77.8%)                          | 1 (8.3%)                        | <0.001* |
| 200-300                               |         | 3 (16.7%)                           | 10 (83.3%)                      |         |
| > 30                                  |         | 1 (5.6%)                            | 1 (8.3%)                        |         |
| <b>Methods of axillary dissection</b> |         |                                     |                                 |         |
| Dissection by scissors                | No. (%) | 12 (66.7%)                          | 2 (16.7%)                       | 0.007*  |
| Dissection by diathermy               |         | 6 (33.3%)                           | 10 (83.3%)                      |         |

their axillary dissection using scissors

Kuroi et al. (25) documented that there was increase in the incidence of postoperative seroma with the use of diathermy because of increased thermal injury. Abbott et al. (26) reported that the use of electro cautery for axillary dissecting is significantly associated with increased seroma formation when compared to dissection by scissors.

In our study we found that there is a statistical significance between seroma formation and the duration of operation only in group A as for those who developed seroma after drain removal their duration of operation ranged from 1.05 to 2.30 hours, while those who did not developed seroma their duration of operation ranged from 1.14 to 2.15 hours

Intra operative blood loss in our study shows a statistical significance in seroma formation mostly in

**Table-6. Significant Univariate Analysis Regarding Seroma Formation In Group B**

|   |         | <b>Non seroma<br/>Mean ± SD<br/>(n = 21)</b> | <b>Seroma<br/>Mean ± SD<br/>(n = 9)</b> | <b>P value</b> |
|---|---------|--|---|----------------|
| <b>BMI (kg/m<sup>2</sup>)</b>             | Mean    | 28.11 ± 4.52                                 | 33.14 ± 5.08                            | 0.012*         |
| <b>Total amount collected</b>             | Mean    | 1239.19 ± 328.44                             | 1832.44 ± 313.86                        | <0.001*        |
| <b>Total amount per day</b>               | Mean    | 112.64 ± 19.83                               | 139.29 ± 19.25                          | 0.002*         |
| <b>Methods of axillary<br/>dissection</b> |         |  |   | 0.042*         |
| Dissection by scissors                    | No. (%) | 12 (57.1%)                                   | 1 (11.1%)                               |                |
| Dissection by diathermy                   |         | 9 (42.9%)                                    | 8 (88.9%)                               |                |

group A for those who developed seroma after drain removal had their intra operative blood loss between 200-300 cc, while for those who did not develop seroma had their intraoperative blood loss less than 200 cc.

Some authors believed that intra operative blood loss, duration of operation and their relationship to seroma formation is of interest but no statistically significant relationship was found. Similarly, the experience of surgeons was not a significant factor. (27) The same observation has also been reported by Funnell et al., (28) who found that seroma formation was not totally avoidable with good technique.

In a study proved by Kuroi et al, patients with chronic disease as hypertension shows a significant influence in seroma formation. (25) Another study done by Kumar et al. (29) who postulated that a higher tendency to continuous exudation at the operative site is responsible for the association between hypertension and seroma formation. In our study no statistical significance was found between two groups and seroma formation regarding those who had chronic medical disease.

A study by Lumachi et al (30) indicated that the tumor size represented the principal factors of seroma formation following axillary dissection in patients underwent surgery for breast cancer, however in our study there was no statistical significance in relation between seroma formation and size of the mass in both groups

With respect to axillary dissection, four studies have consistently indicated that the number of removed LNs does not influence seroma formation (31, 32, 23). As in our study there was no statistical significance between number of lymph node removed and the amount of seroma formation in two groups, also one study has demonstrated that the extent of axillary dissection does not affect seroma formation. (33) On the other hand, a randomized control trial (RCT) of Purushotham et al. (34) has demonstrated that sentinel LN biopsy (SLNB) is associated with significantly less seroma formation than conventional axillary dissection.

In a study by Grobmyer et al. Neo-adjuvant chemotherapy was performed in 18 patients, of whom 6 developed seroma (P=0.030) (35). Found no association between number of drains count and seroma formation, similar to our study.

Different studies suggest different seroma reduction methods. (36) One method to reduce seroma formation is by inserting single axillary drain. There is controversy

concerning treatment and prevention roles of drain, and also the number of drains. (37)

Ebner et al., in a retrospective study has shown insignificance between patients with and without drains after MRM surgery regarding complications (38) Advantages and disadvantages of multi-drain insertion have been examined in some studies. In a retrospective study by Saratzis et al., have evaluated women undergoing MRM in three groups of one, two, and three drains. Results showed insignificant differences in volume of seroma produced among the three groups. (39). in a clinical trial, Puttawibul et al. (40) compared one and two drains in patients undergoing MRM. Same as our study, their results revealed insignificant differences in seroma formation, volume of aspirated liquid, or complications after surgery.

The study by Hashemi et al. (19) showed that seroma occurred in 35% of patients. In multivariate logistic regression analysis, an association of postoperative seroma formation was noted with modified radical mastectomy (OR=2.83, 95% CI 1.01–7.90, P=0.04). No other factor was found to significantly affect the seroma formation after breast cancer surgery. No association between drain count and seroma formation. Which is similar to our study

The post-operative day at which our patients removed their drain was variable and in our study there was no statistical significance in both groups between those who developed seroma and those who did not in relation to the post-operative day at which patient removed their drain

Several randomized control trial (RCT) shows statically significance comparing timing of drain removal and seroma formation. For example, in a study comparing removal of the drain on the fifth post-operative day with removal on the eighth post-operative day (POD), the incidence of seroma formation was significantly high in the former (41). However, in that study, the drain was also removed when drainage volume fell to 30 ml or less per day for 2 consecutive days, and the actual day of drain removal between two groups was not provided. In contrast, in two RCTs comparing drain removal on the fifth POD and removal when daily drainage volume became minimal (42,43), the timing of drain removal did not affect seroma formation.

In the study by Inwang et al. (42) drains were usually removed at the 10th to 14th POD, while the actual day of drain removal was not reported in the study by Ackroyd et

al. (43). On the other hand, evidence was inconclusive when seroma formation was compared between drain removal on the first or third POD, and when drainage volume fell to a minimal level (44, 45, 46, 47). In two RCT (44, 45), early removal of drains increased seroma formation, whereas two other prospective studies did not find a significant association (46, 47).

In a cohort study, compared duration of drain stay. Showed that incidence of seroma increases with short-term axillary drain, and recommended long term axillary drainage for patients undergoing MRM surgery. (48) Which is statistically insignificant compared to our study.

In a study made by Abbott et al. (26) 134 patients underwent mastectomy between 2007 and 2011; it was documented that the overall complication rate was 21.6%. The complications were in the form of superficial wound infection, deep tissue infection, superficial epidermolysis, edge flap necrosis, and hematoma formation.

In our study hematoma formation shows a statistical significance between two groups and about 6 patients developed hematoma collection in group B those patients most of them had body mass index ranged from 25 to 38 and almost had hypertension. The hematoma was diagnosed by clinical and ultrasonographic examination, and evacuated under local anesthesia by incision and drainage and patients followed up regularly for one month and no recurrence was noticed.

A statistical significance was found between two groups compared to seroma formation regarding total amount collected and total amount per day.

Another study found that the volume of fluids collected during the first 24h postoperative predicts total seroma volume and total time of seroma treatment. Statistical analysis revealed a significant correlation between these parameters. More to the point, they found that collection of less than 130 ml of fluids on the first postoperative day was related to lower total seroma volume and shorter total time of seroma treatment.

## Conclusion

It was found that one drain insertion after modified radical mastectomy (MRM) surgery is as effective as two drains, however some patients experience less seroma formation and early drain removal using single axillary drain.

Also it was found that single axillary drain is suitable for those patients who had their BMI ranged from 18, 5 to 24, 9. patients who had their axillary dissection using scissors, patients with short duration of operation (not more than 1.30 hour), and patients with intra operative blood loss not more than 200 cc. while two drains (axillary and pectoral drain) was found to be suitable in patients with BMI more than 40, patients who had their axillary dissection using diathermy, patients with prolonged duration of operation (more than 1.30 hour) and patients who had intra operative blood loss more than 200cc.

We postulated that combining INR with the classic Blatchford score could augment its predictive power.

Testing our hypothesis through the collected data was done. The mean calculated combined Blatchford-INR score was  $6.7 \pm 5.0$ . It was evident that combined Blatchford-INR score had the highest sensitivity and specificity for prediction of unfavorable outcomes in patients with UGIB. A cutoff value of  $\leq 12.0$  predicts complete cure with a sensitivity 94% and specificity 100%, whereas a cutoff of  $\geq 13$  predicts rebleeding with sensitivity 100% and specificity 92.7% and a cutoff of  $\geq 15$  predicts mortality with a sensitivity of 100% and specificity of 89.8%.

## Recommendations:

Blatchford score as a prognostic tool in emergency and gastroenterology departments, and have high sensitivity and specificity than RS for predicting outcomes.

Combining INR with the classic Blatchford score could augment its predictive power. It was evident from our results that combined Blatchford-INR score had the highest sensitivity and specificity for prediction of unfavorable outcomes in patients with UGIB. A cutoff value of  $\leq 12.0$  predicts complete cure with a sensitivity 94% and specificity 100%, whereas a cutoff of  $\geq 13$  predicts rebleeding with sensitivity 100% and specificity 92.7% and a cutoff of  $\geq 15$  predicts mortality with a sensitivity of 100% and specificity of 89.8%. However, these findings require external validation through other prospective studies. We need more studies for two scores and orientation to hemoglobin and urea as two factors can change from admission as first presentation and follow up in hospital, need to detect more factors can be added to scores.

## Conflicts of Interest

Authors declare that there is no conflict of interests regarding the publication of this paper.

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