**A study of selective chest X-ray post chest drain removal following lung resection**

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**Visual abstract:**

* ***Key question:***
1. The aim of this study was to discover whether it is safe to selectively carry out a chest X-ray post chest drain removal following lung surgery and explore the probability of needing a chest drain reinsertion.
2. To identify the effectiveness of a chest X-ray post chest drain removal.
3. To evaluate the financial impact for carrying out a routine chest X-ray following chest drain removal in the thoracic department of the hospital.
4. To formulate recommendations for the future management of thoracic patients, such as whether to carry out routine chest X-ray after the chest drain removal.
* ***Key findings:*** A total of 2050 patients were included in this study and 90% of them were clinically stable after their chest drain removed. Only 21 (1%) patients required a chest drain reinsertion, 20 out of the 21 patients (95%) experienced some degree of respiratory difficulties, such as: hypoxia, dyspnoea, tachypnoea or/and reduced pulmonary sounds, which warranted further investigation leading to a chest drain reinsertion. The remaining patient of the group of 21 did not show any signs and/or symptoms but had the drain reinsertion based on CXR findings, which may or may not have been necessary.
* ***Take-home message:***Performing a chest X-ray post chest drain removal following lung resection is necessary only if the patient who have respiratory or hemodynamic instabilities or following any concerns of surgeons by reasoning of patient’s comorbidity and findings from the procedure. By following this recommendation in this study, over ninety percent of the Thoracic patients who had a “routine” Chest X-ray after a chest drain removal following lung resection would have had their X-ray withheld without compromising the patients’ care.

In patients undergoing thoracic surgery and had a lung resection, clear objective symptoms and signs accompanied clinically significant pneumothorax, pleural effusion, or surgical emphysema after their chest drain removal. Selective performance of chest X-rays following chest drain removal might lead to a significant cost saving alongside other benefits such as earlier discharge, a reduction in exposure to radiation and unnecessary interventions in asymptomatic patients.

**Abstract:**

*Objective:* The purpose of this retrospective study is to determine the safety and efficacy of selectively performing a chest X-ray post chest drain removal following lung resection. In a large thoracic centre in the southern England, there were four surgeons. One of them did not perform a routine chest X-ray following a chest drain removal for patients under his care unless clinical signs and/or symptoms indicated it was necessary, but the other three did a routine Chest X-ray.

*Methods*:A total of 2083 patients were identified within this study, and they were divided into two groups. Those who selectively had a chest X-ray (Group 1, *n* = 444) and those who had a routine chest X-ray (Group 2, *n* = 1639). Medical records were retrospectively reviewed from the hospital database.

*Results*: A total of 90% patients within this study were clinically stable after their chest drain removed. There were only 21 (1%) patients (8 in Group 1 & 13 in Group 2) needed a chest drain reinsertion. Twenty (95%) out of those 21 patients developed some degree of respiratory difficulties and/or haemodynamic instabilities.

During the study period, £14,166 could have been saved if the Group 2 patients did not have their chest X-ray routinely following their chest drain removal.

*Conclusion*: A chest drain reinsertion in patients following its removal was relatively rare and the decision for chest drain reinsertion was based on clinical signs, symptoms, and the surgeon’s clinical judgement. A chest X-ray should be a guide for clinicians to use to confirm their clinical suspicion and to quantify the size of the pneumothorax/pleural effusion/surgical emphysema but should not be performed as a routine.

**Keywords:**Chest X-ray; lung resection; post chest drain removal.

**Abbreviations:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Abbreviation** | **Full description**  | **Abbreviation** | **Full description** |
| ACDS | Ambulatory chest drains system  | LUL | Left upper lobectomy |
| AKI | Acute kidney injury | NHS | National health service |
| ANP | Advanced nurse practitioner | RE | Readmission |
| AS | Asymptomatic | REP | Repeat |
| CD | Chest drain | RLL | Right lower lobectomy |
| CI | Chest infection | RML | Right middle lobectomy |
| CT | Computerised tomography | RUL | Right upper lobectomy |
| CXR | Chest X-ray | RLBiL | Right lower bilobectomy |
| DC | Discharge | RUBiL:  | Right upper bilobectomy |
| DNA | Deoxyribonucleic acid | SCTS | Society for Cardiothoracic Surgery |
| FAF | Fast atrial fibrillation | SF | Satisfactory |
| FD | Following day | TB | Tuberculosis |
| IV  | Intervention | VATS | Video assisted thoracic surgeryt |
| LLL | Left lower lobectomy |  |  |

**Introduction:**

It is common practice to carry out a chest X-ray (CXR) in patients after chest drain removal following their lung resection surgery. The purpose of the CXR is to rule out a pneumothorax, check lung re-expansion and any other abnormality following the operation.

There is growing evidence from literatures that a CXR is not routinely needed following the removal of a chest drain (CD) in adult patients who have had a CD inserted following a lung resection, trauma, or spontaneous pneumothorax etc [1][2][3][4]. Despite this evidence, there is still debate in practice as to whether it is necessary to carry out a routine CXR following a CD removal.

In a thoracic centre in the southern England, there are four surgeons. One of them does not perform a routine CXR following a CD removal for patients under his care. For those patients, the nursing staff will monitor them for 2 - 4 hours following the CD removal. After an Advanced Nurse Practitioner (ANP) has examined them, they will be discharged home if they are clinically stable. If there were clinical signs and/or symptoms such as shortness of breath, desaturation or cardiovascular instability etc, a CXR will be performed and acted upon. However, the other three surgeons still request a routine CXR for their patients, although there are no current studies providing evidence that demonstrates clinical benefit [1]. This practice is not only a burden for nursing staff and the radiographers in addition to their busy workload, but also has some financial impact for the hospital.

The decision to obtain a CXR after CD removal is dependent on surgeon preference but not on any specific disease process or other clinical determinant or evidence-based practice. **NHS [5] Finding the Evidence** stated – that when health professionals make a treatment decision with their patient, they should base it on their clinical expertise, the preferences of the patient, and the best available evidence. It has been confusing to some patients and health care professionals as to why the same procedure applies to some patients but not others. The routine use of CXR following the CD removal have recently been challenged [1][2][3][4][6][7][8].

One of the complications following CD removal is the recurrence of pneumothorax. Patients may be asymptomatic, develop shortness of breath, or in extreme cases have tension pneumothorax. Small pneumothoraxes in asymptomatic patients that are clinically stable can be managed with clinical observation and followed up with CXR to check lung re-expansion and resolution of pneumothorax [3]. In symptomatic patients or patients with a large pneumothorax, a CD will be inserted to allow lung re-expansion. CXR following the removal of the CD should not be performed routinely but should preferably be based on the good clinical judgement and discernment of the surgeon [4].

Cunningham et al [6] stated that most iatrogenic pneumothoracis resulting from chest drain removal are atmospheric in origin, asymptomatic, and can be observed. From personal experience, the CXR post CD removal rarely results in change to the clinical management of the patients.

In order to investigate this observation further, a hypothesis was set up that stated that the selective carrying out of a CXR post CD removal following a lung resection is safe and cost effective. If routine use of CXR after CD removal does not frequently result in a change in patient management, then a CXR should only be obtained based upon clinical indication in this population of patients.

 A retrospective quantitative review of medical records from the hospital e-document database was conducted on all adult thoracic patients with a CD placed following their lung resection in a five-year period. A total of 2083 medical records of patients who had undergone lung resection between January 2013 and December 2018. were evaluated. The patients were divided into two groups based on the surgeons: Group 1 (*n*=444), involved selective performance of a CXR post CD removal (1 surgeon). For these patients, the decision to perform a CXR after the CD removal, following their lung resection was dependent on the patient’s clinical presentation, the surgeon’s preference according to the patient’s co-morbidity or intraoperative findings during the procedure and/or any complications of the patient’s recovery following their operation. Group 2 (*n*=1639) included patients for whom a routine CXR was performed following a CD removal (the other 3 surgeons).

**Materials and methods:**

This study was approved by the Clinical Governance Board (CGB) at the hospital (SEV/0107, 26/06/2019) and the University of Southampton Faculty of Environmental and Life Sciences Ethics Committee for NHS service evaluation or audit (Ethics ID: 52194, 30/09/2019). Hart [9] stated that the two main ethical issues are firstly that the participants in the research must give their fully informed consent and secondly that they are not harmed as a result of their participation. Data for this study was collected retrospectively from the hospital database, and therefore no patients who were included in the research would not be physically harmed as a result of their participation, since it was based solely on existing records. A consent was signed by all the patients prior to their thoracic procedure which stated that the patients understood that all the information collected for the procedure could be used for research studies and would be subject to research ethic’s approval and to national standards of practice.

In terms of the inclusion/exclusion criteria, the data from patients who had had a lobectomy, bullectomy and wedge resection were included in the study and the patients who had prolonged air leak following thoracic procedure, trauma, empyema, pneumonectomy, mediastinotomy, lung biopsy, pleural biopsy and lung volume reduction surgery were excluded, due to the differences in the management of the CD. The patients who met the inclusion criteria, but where it was not possible to obtain detailed information of the date of the CD removal or the CD that were managed outside the thoracic unit (*n*=18 in Group 1 and *n*=15 in Group 2), were also excluded from the study.

The data collected included patients’ demographic information, types of thoracic procedure, length of chest drain in situ and hospital stay, distribution of re-evaluation which included signs and symptoms and CXR findings, date of operation, date of chest drain removal, chest X-ray findings, date of discharge, the reasons for selecting some patients to perform a CXR post chest drain removal in Group 1 and a further emergency visit or hospital admission because of surgical complications.

**Results:**

In this study, a total of 2083 patients fulfilled the inclusion criteria, and 33 patients who met the inclusion criteria but had to be excluded from this study because of the data on the CD removal date was not available or because the CD had been managed outside of the thoracic unit. A total of 2050 patients were selected in this study, Group 1 (n = 426), selective performance of CXR following CD removal, and Group 2 (n = 1624), routine CXR post CD removal. The number of patients and their age at the time of the operation of both groups are displayed in Table 1.

**Table 1**

**Patients’ Demographics**

|  |  |  |
| --- | --- | --- |
| **Demographic** **Data** | **Patient Population** |  |
|  | Group 1(n = 426) | Group 2(n = 1624) | Total(n = 2050) |
| **Female – number** **(%) of patients** | 222 (52%) | 795 (49%) | 1017 (50%) |
| **Male – number** **(%) of patients** | 204 (48%) | 829 (51%) | 1033 (50%) |
| **Age – years****(Mean)**  | 17.3 – 93.2(mean 63.5)  | 16.2 – 90.3 (mean 63.8)  | 16.2 – 93.2(mean 63.7) |

All the surgical procedures were performed under general anaesthetic with a video assisted thoracoscopic surgery (VATS) approach, although some of them were converted to thoracotomy. In both groups, all the CXR were reviewed by an experienced cardiothoracic registrar or a consultant, and the findings of the CXR were documented in the patients’ medical records.

The method of removal of the CD was standardised. All the nurses performing the procedure had gained local competency prior to carrying out the procedure. The CD was double clamped, and it was removed at the end of the inspiration with the patient holding their breath whist the CD was pulled out. An occlusive dressing was applied to the drain site immediately subsequent to the drain removal. All the patients were monitored closely for any signs or symptoms of respiratory or cardiovascular compromise.

The indications for CXR after the CD removal in Group 1 patients were symptoms of dyspnoea, tachypnoea, low saturation on pulse oximeter, abnormal findings in chest examination, hemodynamic instability, surgeon’s preference according to patients’ co-morbidity or intraoperative findings and/or any complications while in recovery following their operation.

The type of thoracic surgery procedure performed during the study period is listed in Table 2. The percentage of the patients who underwent lobectomy, wedge resection, bullectomy and talc/abrasion pleurodesis operations are similar within these two groups. Segmentectomy was included in the wedge resection category.

**Table 2**

**Type of Thoracic Surgery Procedure Performed**

|  |  |  |
| --- | --- | --- |
| **Type of Procedure** | **Group 1****No. (%) of patients****(n = 426)**  | **Group 2****No. (%) of patients****(n = 1624)** |
| **Lobectomy (includes RUL, RML, RLL, RUBiL, RLBiL, LUL & LLL)** | 200 (47%) | 862 (53%) |
| **Wedge resection (includes segmentectomy) in RUL, RML, RLL, LUL & LLL)** | 181 (42%) | 583 (36%) |
| **Bullectomy + Talc/ abrasion pleurodesis** | 45 (11%) | 179 (11%) |

Note: LLL = Left lower lobectomy. LUL = Left upper lobectomy. RLL = Right lower lobectomy. RLBiL = Right lower bilobectomy. RML = Right middle lobectomy. RUL = Right upper lobectomy. RUBiL = Right upper bilobectomy.

The details of the management of the patients in these two groups is displayed in Figure 1. In Group 1, forty-two patients (10%) were selected for a CXR following the CD removal due to their comorbidity, high BMI, current smoker, findings from the surgery, complications from the procedure and/or recovery post the operation. Thirty (7%) patients among those 42 patients post drain removal CXR did not provide any additional information to alter the management. Twelve patients (3%) who were selected to have CXR following the CD removal had abnormal findings on CXR, seven of them (2%) had small pneumothorax or atelectasis without any clinical compromises and consequently they were discharged from the hospital. Five patients (1%) needed further intervention. Two patients (0.4%) among those five patients had moderate pneumothorax on the CXR but they were clinically stable and had repeated CXR on the follow day. The size of the pneumothorax remained unchanged; therefore, they did not need any further intervention. One patient’s (0.2%) CXR showed large chest wall haematoma. He went on to have chest computerised tomography (CT) according to the surgeon’s plan, no further intervention was required. Two out of those five patients (0.4%) needed CD reinsertion because of pneumothorax and/or surgical emphysema, the CDs were removed after two to six days.

The remaining 384 patients (90%) in Group 1, did not have a CXR following their CD removal, 17 of them (4%) developed some respiratory difficulties, such as dyspnoea, tachypnoea, low saturation on pulse oximeter, abnormal findings in chest examinations or hemodynamic instability. All these 17 patients had warranted a CXR. All the CXR were reviewed by an experienced thoracic registrar or a consultant. In thirteen (3%) out of those 17 patients’ the CXR was satisfactory, which included 3 patients who had a small to moderate pneumothorax, but there was no clinical compromise and no indication for intervention, as a result of this, they were discharged. However, 1 (0.2%) of those 3 patients was readmitted two days after the discharge due to worsening dyspnoea. A CXR was performed in the emergency department which demonstrated that the pneumothorax had increased in size considerably compared to the CXR prior to discharge. A CD was inserted as the result of the large pneumothorax. The patient was discharged six days later with the CD connected to an ambulatory chest drainage system (ACDS). The CD was removed two weeks after the discharge. Five other patients (1%) out of the 17 who had CXR required chest drain reinsertion due to pneumothorax and/or surgical emphysema. The CD was subsequently removed after three to six days with no additional complications.

The remaining 367 patients (86%) who did not have CXR following the CD removal in Group 1 were monitored in hospital over two hours. They remained clinically well, and no abnormalities were found on auscultation of their chest, and therefore they were deemed to be fit for discharge.

In Group 2, a total of 1467 patients’ (90%) a CXR were assessed as satisfactory after the CD removal, and 157 patients (10%) had abnormal finding from the CXR. Forty (2%) out of 157 patients did not need any additional intervention despite the abnormal findings of their CXR. The remaining 117 patients (8%) who had abnormal CXR post chest CD removal required further intervention. Five of them (0.3%) needed reinsertion of a CD due to the finding of large pneumothorax and/or surgical emphysema on the CXR. One hundred and six patients (7%) had repeated CXR on the following day, and 98 (6%) of them had unchanged or improved pneumothorax, their clinical presentation and chest auscultation remained unchanged. Eight (0.5%) out of 106 patients required CD reinsertion after the repeat of a CXR due to worsening pneumothorax and/or surgical emphysema. Six (0.3%) of those 117 patients were discharged with a plan to repeat a CXR in one week following their discharge from the hospital, and all their CXR showed unchanged or some improvement comparing to the CXR prior to discharge. Among those 117 patients, a total of 112 patients (7.6%) had repeated CXR on the following day or within one week, the CXR of 104 (7.1%) patients remained the same or improved.

A total of 13 patients (0.8%) needed CD reinsertion in Group 2. Twelve out of those thirteen patients (0.8%) had some degree of respiratory instabilities (Table 4). There was only one patient (0.06%) who needed CD reinsertion did not have any clinical signs or symptoms to indicate his pneumothorax had worsened. The indication of the CD reinsertion for him was clinical judgement from the worsening pneumothorax of the repeated CXR.

Figure 1. Impact of post chest drain removal CXR on patient management after lung resection

The length of time while the chest drain was in situ, number of days of hospitalisation post CD removal and total number of days in hospital is displayed in Table 3. In Group 1, the length of CD in situ was 0.25 day shorter than Group 2, and the number of days in hospital following the CD removal in Group 1 was 0.19 days shorter than Group 2. The total number of days in hospital after operation was 0.22 days shorter in Group 1 compared to Group 2 (Table 3).

The reason for delayed discharge from both study groups was similar, which

Included social issues, chest infection (CI), constipation, urinary retention, decreased mobility post operation, awaiting investigation result such as tuberculosis (TB),

atrial fibrillation (AF), hyponatraemia, acute kidney injury (AKI) and pain.

**Table 3**

 **Length of chest drain in situ and inpatients days post chest drain removal**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Group 1****(n = 426)****Days** | **Group 2****(n = 1624)****Days** | **P value****Student T Test** |
| **Chest drains in situ**  | 0 – 29(mean 1.93) | 0 – 30(mean 2.18) | ? |
| **Inpatients post drain removal** | 0 – 19(mean 1.67) | 0 – 48(mean 1.86) | ? |
| **Total in hospital stay after operation** | 0 – 29(mean 1.80) | 0 – 48(mean 2.02) | ? |

There were eight patients (2%) in Group 1 compared with thirteen patients (1%) in Group 2, who required CD reinsertion due to pneumothorax and/or surgical emphysema and/or pleural effusion. All the eight patients (100%) in Group 1 and twelve patients (92%) in Group 2 had shown some degree of respiratory difficulty (Table 4). Only 1 patient (5%) out of the 21 who needed CD reinsertion did not show any signs or symptoms of deterioration in both these groups.

**Table 4**

**Distribution of re-evaluation: signs and symptoms, CXR findings and resulted interventions**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Group 1:****Selective CXR****n = 8 (2%)** | **Group 2:****Routine CXR****n = 13 (1%)** | **Total patients****n = 21 (1%)** |
| **Chest drain reinsertion** |  |  |  |
| **Pneumothorax** | 4 (a) (50%) | 8 (c) (61.5%) | 12 (57%) |
| **Pleural effusion** | 1 (12.5%) | 1 (7.6%) | 1 (5%) |
| **Surgical emphysema** | 2 (b) (25%) | 1(d) (7.6%) | 3 (14%) |
| **Pneumothorax and surgical emphysema** | 1 (12.5%) | 3 (23%) | 4 (19%) |
| **Signs and Symptoms** |  |  |  |
| **Dyspnoea** | 6 (75%) | 8 (61.5%) | 14 (67%) |
| **Tachypnoea** | 4 (25%) | 6 (46.1%) | 10 (48%) |
| **Low O2 Saturation** | 6 (75%) | 9 (69%) | 15 (71%) |
| **Haemodynamic instability** | 2 (25%) | 3 (23%) | 5 (24%) |
| **Reduced pulmonary sounds** | 6 (75%) | 11 (84.6%) | 17 (81%) |

a. One of the patients developed dyspnoea 5 days post chest drain removal. CXR demonstrated pneumothorax. Chest drain was reinserted.

b. One of the patients was discharged 4 hours post chest drain removal, and he was readmitted 2 days later with surgical emphysema, a chest drain was reinserted.

c. One of the patients developed dyspnoea and low O2 saturation 2 days post the chest drain removal, and one of them developed same symptoms 5 days following the chest drain removal. Both had repeated CXR after the development of their symptoms, which showed pneumothorax had worsened compared to the previous ones. Both had a chest drain reinserted.

d. The patient developed the symptoms 2 days post chest drain removal and a chest drain was reinserted.

**Discussion:**

Previous literature suggests that the performance of a CXR after a CD removal in thoracic patients does not support clinical decision making and that clinical signs and symptoms combined with clinical judgement are the main reason that led to an intervention and should be recommended for future practice [1][2][3][4][6][7][8]. However, the evidence of omitting a routine CXR after CD removal following lung resection in adult patients was limited. The result of this study has provided some valuable evidence in line with the hypothesis that selective performance of a CXR post chest drain removal following a lung resection is safe and cost effective.

A total of 21 (1%) patients (8 patients in Group 1 and 13 patients in Group 2) within this study had CD reinsertion (Figure 1), twenty out of the 21 patients (95%) experienced some degree of respiratory difficulties (Table 4), which warranted further investigation leading to a CD reinsertion. There was only one among those 21 patients (5%) who required a CD reinsertion who did not show any signs and/or symptoms but had a CD reinsertion based on CXR findings, which may or may not have been necessary.

CD is an integral step after a thoracic operation and necessary for the evacuation of fluid or air from the pleural space. Carrying out a routine CXR after a CD removal is the standard of care in many institutions [8]. The yield of routine CXR regarding recurrent pneumothorax, pleural effusion and/or surgical emphysema requiring CD reinsertion was relatively low in this study; only 1% of patients in Group 2 and 2% in Groups 1 had CD reinsertion after the CD removal, for which 95% of them developed respiratory or/and haemodynamically instabilities to merit that decision. This study has provided some evidence that clinical signs and symptoms combined with clinical judgement has led to an intervention and should be recommended for future practice, this has been supported by the literatures [1][2][3][4][6][7][8]. The probability of a patient needing a CD reinsertion after chest drain removal following a lung resection is very low based on these findings.

In the vast range of health care expenditures, performing a CXR is relatively cheap, however, as the budget of each NHS hospital has been tightened in the last 2 decades, any investigation should be evidence based and it is the healthcare professional’s responsibility to preserve our resources. **NHS [5] Finding the Evidence** stated: “when health professionals make a treatment decision with their patient, they should base it on their clinical expertise, the preferences of the patient, and the best available evidence.”

During the study period, £14,166 would have been saved from just the cost of a CXR if the Group 2 patients did not have theirs routinely following the CD removal. The CXR savings did not include the cost of nursing staff, radiographers, porters, ward clerks and receptionists’ wages, which would add a remarkable amount of savings in addition to the figures already calculated in this study. This will have a financial impact for the trust in addition to being a burden for those staff on top of their busy workload. In addition to this, patients exposure to radiation would have been unnecessary if they did not develop any clinical signs and symptoms following their CD removal.

X-Ray is based on [ionizing radiation](https://www.cancer.gov/Common/PopUps/popDefinition.aspx?id=CDR0000430698&version=Patient&language=English) which has enough energy to damage deoxyribonucleic acid (DNA) and cause cancer [10]. Radiation-induced cancers typically do not occur until one or two decades or even longer after exposure. Thus, any increase in cancer occurrence due to medical imaging may not be expected to be evident for many years after exposure. Recent European Guidelines stated that the long-term risk associated with radiation exposure should be considered in the risk-benefit assessment behind appropriate prescription of diagnostic testing [11].

The findings of this study contribute to a clear understanding of why selectively performing a CXR post CD removal following lung resection is safe and cost effective. This finding fits in with existing knowledge [1][2][3][4] and contributed some additional evidence to guide future practice.

**Conclusion:**

In summary, the result of the study indicated that performing a CXR post CD removal following lung resection is necessary only if the patient has respiratory or hemodynamic instabilities or following any concerns of surgeons by reasoning of patient’s comorbidity and findings from the procedure. By following this recommendation in the population of the patients in this study, ninety percent of CXRs in Group 2 could have been eliminated without compromising the patients’ care, and it could have led to an early discharge and reduction of radiation exposure and potential cost savings in 1000s of pounds

In this study, thoracic patients who had lung resection operation, objective signs and symptoms usually accompanied clinically significant of pneumothorax, pleural effusion, or surgical emphysema after CD removal. Selective performing of CXR following CD removal might lead to a significant cost saving, or other benefits such as earlier discharge, a reduction in exposure to radiation, unnecessary interventions in asymptomatic patients. These results have provided some valuable evidence for future prospective studies to perform CXR after CD removal only for symptomatic patients or those patients with tenuous comorbidities.

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**Conflict of interest statement:**

We declare that there are no relevant financial or non-financial competing interests to report.

**Author contribution statement**

The authors confirm contribution to the paper as follows:

Study conception and design: Xiao Hui Liu. Aiman Alzetani.

Data collection: Xiao Hui Liu.

Analysis and interpretation of result: Xiao Hui Liu. Aiman Alzetani

Draft manuscript preparation: Xiao hui Liu. Aiman Alzetani

All authors reviewed the results and approved the final version of the manuscript.

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