





# Bleeding Complications in Uremic Patients After Ultrasound-Guided Central Venous Catheter Placement

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**Introduction:** Bleeding associated with elevated blood urea nitrogen (BUN) is a known complication. Patients with uremia require a central venous catheter insertion by dialysis. The relation between BUN and bleeding complications during central venous catheter insertion is not yet clear.

**Objective:** We described the frequency of complications associated with central venous catheter implantation in uremic patients and evaluated the statistical relationship between bleeding complications and catheter type, number of punctures, and catheter insertion site. Also, we determined if any value of BUN is associated with bleeding complications.

**Methods:** We included patients with a serum value of BUN >70 mg/dl that required insertion of a central venous catheter. The quantitative variables were expressed through the measure of central tendency. A bivariate analysis and a ROC curve were performed.

**Results:** A total of 273 catheters were included in this study. Bleeding complications were detected in 69 cases (25.3%), and local bleeding was the most frequent complication in 51/69 cases. Statistically significant association was not established. We did not find a specific cut-off value directly related to BUN levels and the rate of complications.

**Conclusion:** Bleeding complications associated with the insertion of central venous catheter and the suspected disorder of hemostasis given by BUN levels >70 mg/dl are common. It was not possible to determine a BUN cut-off value to predict complications. The association analysis was not conclusive. High BUN levels should not be considered a high-risk condition for central venous cannulation under ultrasound guidance performed by trained personnel.

**Keywords:** central catheterization, vascular catheter, ultrasound imaging, blood coagulation disorders, blood urea nitrogen

## Background

Uremia is a clinical condition associated with worsening renal function secondary to acute or chronic renal failure, systemic infection, cancer, and other diseases. Uremic patients can develop bleeding complications due to platelet aggregation dysfunction, Von Willebrand factor dysfunction, loss of erythrocyte mass, and high levels of cAMP (cyclic adenosine monophosphate) or cGMP (cyclic guanosine monophosphate).<sup>1–9</sup>

High BUN levels are associated with gastrointestinal bleeding<sup>11,12</sup> or spontaneous brain bleeding and increased bleeding episodes in trauma patients.<sup>10</sup>

Despite the potential risk of bleeding complications due to uremic coagulopathy,<sup>52–56</sup> uremic patients frequently require the implantation of a central venous catheter to provide renal replacement therapy or invasive treatment.

In general, risk of major and minor bleeding associated with a central line placement in patients with coagulation abnormalities is highly variable, with bleeding rates ranging between 0% and 32%.<sup>13–15</sup> However, the ultrasound guide for insertion of a central venous catheter reduces the number of punctures, provides a greater chance of success in the first attempt, reduces the risk of arterial puncture, and reduces the incidence of hematomas in non-compressible places.<sup>10,16–19</sup>

Bleeding complications after the insertion of a central venous catheter in uremic patients are relatively uncommon.<sup>14,20–23</sup>

The aim of this study was to describe the frequency of complications associated with the insertion of central venous catheters in patients with a suspected disorder of hemostasis given by levels of  $>70$  mg/dl.<sup>19</sup> Additionally, we performed a bivariate analysis to determine possible relationship between catheter type, number of puncture, catheter insertion site and bleeding complications. Finally, we evaluate the possible utility of a cut-off value for serum BUN associated with bleeding complications related to the procedure.

## Materials and Methods

### Data Source

This retrospective descriptive study was conducted in an emergency department of a highly complexity University Hospital (Fundación Valle del Lili) in Southwestern Colombia between January 2013 and July 2019. Patients with serum urea nitrogen levels  $>70$  mg/dl were selected. We defined the value of serum BUN of the results obtained by Jamale<sup>19</sup> for the initiation of renal replacement therapy defined.

The ethics committee in biomedical research at University Hospital (Comité de Ética en Investigación Biomédica de la Fundación Valle del Lili) approved this study (Register No. 210-2018, approved on August 01, 2018. Institutional act No. 15 of August 01, 2018, protocol number 1279). This study applying the declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. This study adhered to the standards of the STROBE guidelines.

This study did not present risk (according to resolution 8430 of 1993 of the Colombian Ministry of Health); since it is documentary in nature, and the researchers do not assign biological, psychological, or social exposures to patients. Therefore, the ethics committee omitted the use of informed consent. All patient data accessed complied with relevant data protection and privacy regulations.

### Study Population

The selected medical records had to meet the following inclusion criteria: 1) age greater than or equal to 18 years, 2) blood samples taken 24 hours before or after insertion of the central venous catheter, 3) BUN  $> 70$  mg/dL, 4) central venous catheter inserted with ultrasound guidance and 5) recording of the procedure data by the specialist who performed the procedure. The professionals who performed the catheter insertion are all emergency medicine specialists with certified training in this ultrasound-guided practice.

All patients who received platelet transfusion 24 hours before the procedure were excluded.

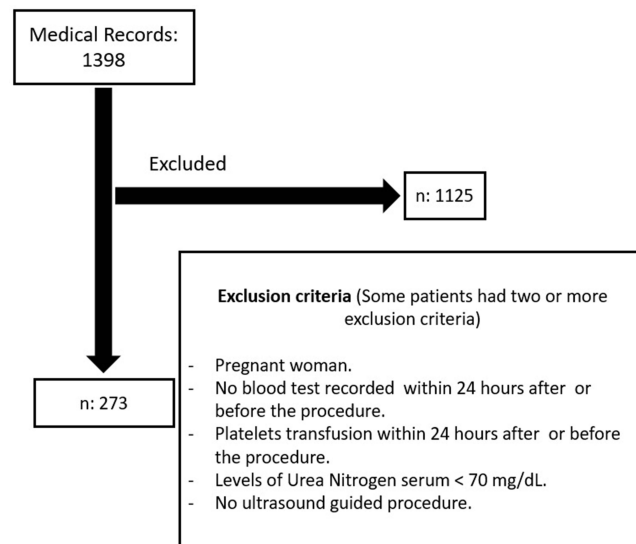
### Statistical Analysis

A descriptive analysis was performed. The normality of the variables was determined through a Shapiro–Wilk test. According to their distribution, the quantitative variables were expressed through the measure of central tendency and dispersion. Categorical variables were described in proportions and compared with Chi-square test or Fisher's test. Receiver operating characteristic (ROC) analysis was applied to determine the threshold value of BUN related to the bleeding complications after catheter insertion.

Bleeding complications were defined as the presence of oozing from the skin insertion site, hematoma that did not require intervention and resolved with manual compression (Grades 1–2), a decrease in hemoglobin level  $\geq 1.5$ g/dL judged to be associated with the catheter insertion or arterial puncture. Coagulopathy factors were documented as a partial thromboplastin time, prothrombin time value in platelets.

## Results

A total of 1398 medical records were reviewed. A total of 273 records of procedures performed (273 inserted catheters) were included and analyzed. (Figure 1). There was a predominance of females, with a median age of 61 years. The most commonly used type of central venous catheter was Mahurkar (n: 184–67.4%), followed by the triple lumen catheter (n: 49–17.9%) and double-lumen catheter (n: 34–12.5%). The internal jugular vein was the most common insertion site



**Figure 1** Study flowchart.

chosen by the specialist (n: 146–53.5%). The success rate in the first puncture by ultrasound guidance was 93%. Chronic kidney disease was the first cause of indication for inserting the catheter (46.2%). The second cause was Sepsis indicated for the management with vasopressors (21.6%). Median of platelet count was 176,000. Median PTT values were prolonged (Table 1).

**Table 1** Clinical Characteristics

<b>Age**</b>	61 (45–71)
<b>Sex, n (%)</b>	
Female	165 (60.4)
<b>Type of central venous catheter, n (%)</b>	
Mahurkar	184 (67.4)
Triple lumen	49 (17.9)
Double lumen	34 (12.5)
Swan ganz	6 (2.2)
<b>Catheter insertion indication, n (%)</b>	
Dialysis	185 (67.8)
Infusion of irritating drugs	73 (26.7)
Invasive monitoring	8 (2.9)
No peripheral access	7 (2.6)
<b>Catheter insertion site, n (%)</b>	
Jugular vein	146 (53.5)
Subclavian vein	67 (24.5)
Femoral vein	58 (21.2)
Femoral artery	2 (0.7)
<b>Number of punctures under ultrasound guidance, n (%)</b>	
1	254 (93)
2	13 (4.8)
3	4 (1.5)
>5	2 (0.7)

(Continued)

**Table 1** (Continued).

<b>Diagnosis at admission</b>	
Chronic kidney disease	126 (46.2)
Infectious diseases	59 (21.6)
Cardiovascular diseases	29 (10.6)
Oncology disorders	28 (10.3)
Hepatobiliary-pancreatic Disease	21 (7.7)
Other	10 (3.7)
<b>Coagulopathy factor</b>	
<b>Blood urea nitrogen***</b>	89.7 mg / dl (80–111.9)
<b>Platelets***, n: 269/273</b>	176,000 (109,000–276,000)
Platelets < 150,000***, n: 110/269	65,000 (14,000–109,500)
Platelets ≥ 150,000***, n: 163/269	257,000 (200,500–342,000)
<b>PT***, n: 178/273</b>	15.1 (12.6–20.5)
<b>PTT***, n: 175/273</b>	32.1 (28.2–44.2)

**Notes:** \*\*Age in years, data represented in average and standard deviation. \*\*\*Data represented in median (interquartile range IQR).

Bleeding complications were detected in 69 cases (25.3%). Local bleeding after the intervention was the most frequent complication in 51/69 cases (73.9%). Post puncture hematoma was documented in 15/67 cases (21.7%) and Arterial puncture in cases 5/69 (7.2%) (Table 2).

The bivariate analysis showed a statistically significant association between the hematoma and catheter type (p:0.016) and, hematoma and catheter insertion site (p: 0.01) (Table 3).

There was no cut-off value for BUN related to a greater probability of bleeding as a complication associated with the procedure (median within the cohort of 89.7 mg/dl and interquartile range between 80 and 111.9 mg/dl) (Figure 2).

## Discussion

In acutely ill patients with elevated BUN levels and the presence of bleeding complications after the ultrasound-guided central venous catheter placement was presented in 26.7%.

Complications after the insertion of a catheter in patients with uremia are common.<sup>24–29</sup> There is a potential risk of complications suggested by pathophysiological mechanisms in patients with elevated BUN levels and the ultrasound-guided central venous catheter placement present.<sup>30–36</sup> We identified patients with a high BUN value without bleeding complications reported. However, 10 patients (12 catheters implanted) presented a BUN value greater than 150 mg/dl and 2 patients reported any bleeding complication. The coagulopathy factors (Partial Thromboplastin Time and Prothrombin time) was altered in one patient.

**Table 2** Complications Related to Insertion of Central Venous Catheter

<b>Complications</b>	
No	204 (73.3)
≥1 (Mechanics or Hemorrhagic)	73 (26.7)
<b>Types of complications</b>	<b>n: 73</b>
<b>Mechanics, n (%)</b>	
Arterial puncture	6 (8.2)
<b>Hemorrhagic, n (%)</b>	
Bleeding at the insertion site	51 (69.9)
Hematoma	15 (20.5)
Hb decrease ≥1.5 mg/dl	1 (1.4)

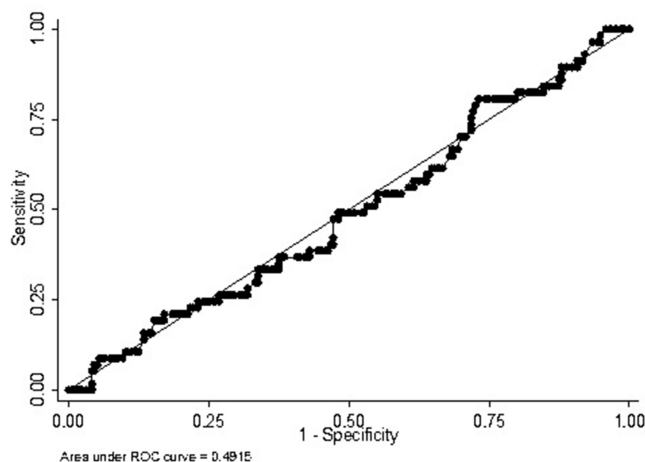
**Table 3** Bivariate Analysis

Catheter type	Bleeding at the Insertion Site		p Value
	Yes: 51	No: 218	
Double lumen (7 French Size)	6 (11.8)	28 (12.8)	0.72
Triple lumen (7 French Size)	10 (19.6)	39 (17.9)	
Swan Ganz (8 French Size)	2 (3.9)	4 (1.8)	
Mahurkar (13.5 French Size)	33 (64.7)	151 (69.3)	
<b>Number of punctures</b>			0.13
1	45 (88.2)	209 (95.9)	
>1	6 (11.8)	13 (6)	
<b>Catheter insertion site</b>			0.69
Jugular vein	24 (47.1)	122 (56)	
Subclavian vein	14 (27.5)	53 (24.3)	
Femoral vein	13 (25.5)	45 (20.6)	
Femoral artery	0 (0)	2 (0.9)	
Catheter type	Hematoma		p Value
	Yes:15	No: 258	
Double lumen (7 French Size)	0 (0)	34 (13.2)	0.016
Triple lumen (7 French Size)	1 (6.7)	48 (18.6)	
Swan Ganz (8 French Size)	0 (0)	6 (2.3)	
Mahurkar (13.5 French Size)	14 (93.3)	170 (65.9)	
<b>Number of punctures</b>			0.74
1	12 (80)	242 (93.8)	
>1	3 (20)	16 (6.2)	
<b>Catheter insertion site</b>			0.01
Jugular vein	8 (53.3)	138 (53.5)	
Subclavian vein	3 (20)	64 (24.8)	
Femoral vein	4 (26.7)	54 (20.9)	
Femoral artery	0 (0)	2 (0.8)	

Previous studies showed that threshold BUN value for distinguishing upper from lower gastrointestinal bleeding was 21.0 mg/dl,<sup>11</sup> and BUN/Cr ratio over 35 mg/dL can predict a gastrointestinal bleeding.<sup>12</sup> Lin et al<sup>10</sup> described BUN levels between 150 and 200 mg/dl of urea nitrogen are associated with spontaneous brain bleeding and increased bleeding episodes in trauma patients. Perhaps, the low number of bleeding complications in our study was related to the fact that the distribution of patients in the cohort had a median BUN of 89.7 mg/dl (IQR 80–111.9 mg/dl). This value of BUN was not severely increased, even when it is among the uremia criteria according to the reference point we used for this analysis ([Supplementary Table 1](#)).

A total of 110/269 patients presented thrombocytopenia (platelets accounts  $<150 \times 10^3/\mu\text{L}$ ) of which 36/110 documented any bleeding complication related to cvc placement. Some authors considered an optimal platelet account  $>50 \times 10^3/\mu\text{L}$  before central venous catheter could be safe.<sup>48</sup> Previous studies have reported a low rate of bleeding complications in patients with thrombocytopenia undergoing central venous cannulation.<sup>14</sup> Our results are according with the literature reported with rates ranging between 0% and 32% after cvc placement.<sup>49–51</sup>

Previous studies have described that the major complications occur about 3% in experimented operator.<sup>47</sup> In our study, one patient (0.3%) presented a major bleeding complication in the first 48 hours after insertion of the catheter. Coagulopathy factors were normal range and value of BUN was 86 mg/dl. Due to profuse bleeding at the insertion site, he required a transfusion of two red blood cell units.



**Figure 2** Area under the receiver operating characteristic (ROC) curve of blood urea nitrogen (BUN) for predicting bleeding complications after placement of central venous catheter.

The use of ultrasound-guided central venous catheter placement decreases the number of complications (especially with a lower risk of arterial puncture) related to bleeding events.<sup>37–40</sup> Randolph et al<sup>41</sup> demonstrated a reduction in the risk of failed attempts compared to the anatomical technique (RR 0.66; 95% CI 0.45 to 0.79) and a reduction in complications (RR 0.22; 95% CI 0.10 to 0.45). Our population is not representative to conclude safety or risk for bleeding complications with ultrasound guidance. However, we considered the useful of ultrasound guidance as a safe procedure for catheter placement.<sup>42–44</sup>

A bivariate analysis was performed. There was a statistically significant association between the hematoma and two independent variables (the type of catheter and catheter insertion site). However, it is not possible to attribute this finding due to the reduced number of patients in the group that presented the event. It is necessary to conduct a study with more cases to determine that this finding is demonstrable. We did not identify a correlation with any cut-off point between high levels of urea nitrogen and any bleeding complication.

Our study has certain limitations. We did not evaluate other variables that contribute to the bleeding complications like medications, platelet transfusion before the procedure and others.<sup>45,46</sup> We considered that a higher sample size for association analysis was necessary to evaluate the relationship between some variables and bleeding complications.

## Conclusion

The frequency of bleeding complications associated with the insertion of central venous catheters in patients with BUN levels >70 mg/dl are common. It is not possible to determine a BUN cut-off value to predict complications and the association analysis is not conclusive.

## Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

## Disclosure

The authors declare that they have no competing interests in this work.

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