TRANSFUSION COMPLICATIONS IN HOSPITALIZED ELDERLY PATIENTS: INTEGRATIVE LITERATURE REVIEW

Complicações transfusionais em pacientes idosos hospitalizados: revisão integrativa da literatura
Complicaciones transfusionales en ancianos hospitalizados: revisión integrativa de la literatura

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ABSTRACT

Objective: to identify the main complications caused by blood transfusion to the health of the hospitalized elderly through the analysis of scientific evidence. Method: integrative review conducted with studies in English from national and international databases published in the period from 2017 to 2021. The main descriptors were “BloodTransfusion”, “Transfusion Reaction”, “Aged” and “Hospitalization”, combined by means of the Boolean operators “AND” and “OR”. Results: 23 studies were included that depicted the main complications of blood transfusion for the hospitalized elderly person. The twelve different complications were allocated into two categories: surgery-related or non-surgical complications. Longer hospital stay, mortality, transfusion reactions, postoperative acute kidney injury and postoperative delirium were among the main achievements. Conclusion: the mechanisms by which complications develop are not yet fully understood, highlighting the importance of encouraging further research on this topic.

DESCRIPTORS: Blood transfusion; Transfusion reaction; Aged; Hospitals.

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RESUMO


DESCLORES: Transfusão de sangue; Reação transfusional; Idoso; Hospitais.

INTRODUCTION

Population aging is a daily reality in most societies. This phenomenon requires restructuring of services and, consequently, adaptation of supply, in addition to the qualification of human resources, ensuring access to meet the health needs of the elderly. As the body ages and undergoes numerous physiological, functional, and biochemical changes, it is not uncommon to observe in geriatric individuals a certain inclination toward reduced hemoglobin concentration. Thus, anemia is a highly frequent problem in long-term care facilities for the elderly, denoting the weakness of the geriatric population.

It is common for elderly people with anemia to be in a state of physical fragility, depressed, and with cognitive decline. Treatment requires careful investigation of the cause, including iron replacement and/or red blood cell transfusion. In order to solve complex conditions, the therapeutic use of blood and its components is one of the therapies recommended in hospitals, and blood transfusion is included in the list of interventions for health recovery. Although it is a beneficial procedure, it is not free of risks, which can be even fatal due to transfusion reactions. Transfusion reactions are those that more routinely represent the adverse effects of hematotransfusion. They can be classified as immediate (in which clinical or laboratory signs occur during the transfusion or up to 24 hours afterwards) or delayed, with the occurrence of clinical or laboratory signs after this period, which can be attributed to the course of the infusion, procedural errors or not, and also inherent to the transfusion safety policy.

When it comes to the implementation of transfusion therapy, the care of the elderly transfused patient is a challenge to health professionals, since physiological characteristics inherent to aging (such as pre-existing morbidities, renal and hepatic impairment, difficulty in self-regulation of the body) contribute to the development of certain post-transfusion complications, including transfusion reactions and others, such as postoperative delirium.

In this process, the nursing team, as it is in charge of the assistance during the whole time, plays a strategic role in transfusion therapy, being able not only to avoid damages, but also to identify and mitigate them. Its performance also contributes to reduce fears and uncertainties through the guidance provided, since the care provided by this team must be surrounded by the educational dimension, contributing to the treatment success and rehabilitation.

Given this context, the study had the following guiding question: “What complications can blood transfusion cause to hospitalized elderly people? In order to obtain answers to the question, the aim was to identify the main complications caused by blood transfusion to the health of the hospitalized elderly through the analysis of scientific evidence.
METHOD

To conduct this study, an integrative literature review was performed. This is a technique that allows the inclusion of experimental and non-experimental studies for the complete understanding of the analyzed phenomenon, in addition to combining data from the theoretical and empirical literature, seeking evidence on the desired subject.\(^{11}\) Data collection and analysis were performed from the steps related to the method: elaboration of the research question; literature search for primary studies; data extraction; evaluation of the studies included in the review; analysis and synthesis of results; and presentation of the review.\(^{12}\) The adoption of these steps is necessary to give the review the necessary methodological rigor.

After choosing the topic, we considered the PICo strategy, an acronym for population, phenomena of interest, context\(^{13}\), to formulate the research question presented. As a population, the elderly hospitalized patient was delimited; regarding the phenomenon of interest, complications were considered; and the adopted context corresponded to blood transfusion.

Additionally, to ensure rigor in conducting the method, the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used.\(^{14}\) A research protocol was prepared and deposited in the figshare repository.\(^{15}\) Data collection was performed in January 2022.

The search was performed according to Medical Subject Headings (MeSH), CINAHL Headings, and Health Sciences Descriptors (DeCS) controlled descriptors. Only publication year filter was added, comprising the period from 2016 to 2021, contemplating current studies. The bases chosen for search were Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System (MEDLINE)/National Library of Medicine (PUBMED), Cumulative Index of Nursing and Allied Health (CINAHL), Scopus and Web of Science.

The main terms used for the search were: "Blood Transfusion", "Blood Transfusions", "Transfusion Reaction", "Hemolytic Transfusion Reaction", "Aged", "Elderly", "Oldest Old", "Geriatric", "Middle Aged" and "Hospitalization". Only publication year filter was added, comprising the period from 2017 to 2021. For the proper correlation of these, the Boolean operators AND and OR were employed.

The criteria for the selection of studies were: original research articles and studies that addressed the complications that blood transfusion can cause to the hospitalized elderly patient, published in English, Portuguese and Spanish, including as study population people aged 60 years or older, available as full text by open or free access, enabling to answer the pre-defined guiding question. Duplicate articles in the databases were excluded, keeping only one; studies related to transfusion complications in people under 60 years of age; editorial letters; reviews; reviews; dissertations; books; and publications in proceedings.

For data extraction, we used an instrument developed for the study, which allowed the collection of information about the identification of the original article, namely: year of publication, author(s) and country of origin of the study; journal of publication of the article; approach and type of study; characterization of the sample according to the number of participants, gender and age; objective(s); and main results.

Regarding the quality of the evidence, we chose the following classification, being the evidence: Level 1 – from systematic review or meta-analysis; Level 2 – derived from at least one well designed randomized controlled trial; Level 3 – obtained from well designed clinical trials without randomization; Level 4 – well designed cohort studies and case-control studies; Level 5 – systematic review of descriptive and qualitative studies; Level 6 – single descriptive or qualitative study; Level 7 – opinion of authorities and/or expert committee report.\(^{16}\)

RESULTS

From the preliminary search, 4,307 publications were identified, of which 200 were from Cinahl (4.7%), 15 from Lilacs (0.3%), 1,688 from MEDLINE/Pubmed (39.2%), 386 from Web of Science (9%), and 2,018 from Scopus (46.8%). Figure 1 shows the selection of articles for each electronic database.

After exclusion of duplicate articles, analysis of titles and abstracts began (n=2,727). Of these, 2,533 studies were excluded. Then, 194 articles were read in their entirety, and 171 were excluded (34 related to the population; 88 to the theme; 3 (3) to the research design; 2 (2) to the type of publication; 5 (5) because the article was not available in its entirety; and 39 because the results were not compatible). In the end, 23 publications were included in the review. Chart 1 shows the selected studies.

The studies were published between the years 2017 and 2021, with 69.6% of them being published between 2019 and 2021. Entirely, the origin was from peer-reviewed academic journals, and articles from 11 different countries were identified. All studies were published in English, with the majority from Asia (34.8%), North America (30.4%), and Europe (30.4%). One (1) study was published in Brazil.

As for the approach, all used quantitative methodology. According to the authors’ description, nine (9) were retrospective cohort; four (4) prospective cohort; two (2) retrospective; four (4) retrospective observational; one (1) retrospective descriptive; two (2) retrospective case-control; and one (1) mixed (retrospective and validation). Therefore, the results found presented level of evidence 4.

The studies included people of both genders, as well as adults aged 60 years or older, although only seven (7) conducted research in populations composed exclusively of elderly people.22,25,30,32,33,35,39

The journal Tranfusion had two (2) articles selected, with one (1) from the year 2017 and one from 2021. Only one (1) article was published in a nursing journal, this being Intensive and Critical Care Nursing from Japan in 2018; four (4) of them were published in journals specializing in hemotransfusion/hemotherapy.
Transfusion complications in hospitalized elderly patients: integrative literature review

Figure 1 – Flowchart (PRISMA) of the selection of included studies. João Pessoa, PB, Brazil, 2022

Chart 1 – Identification code and title of the selected studies. João Pessoa, PB, Brazil, 2022

<table>
<thead>
<tr>
<th>Article</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>E17</td>
<td>Demographic and epidemiologic characterization of transfusion recipients from four US regions: evidence from the REDS-III recipient database.</td>
</tr>
<tr>
<td>E18</td>
<td>Predictive factors for length of hospital stay following primary total knee replacement in a total joint replacement centre in Hong Kong.</td>
</tr>
<tr>
<td>E19</td>
<td>Risk factors for postoperative delirium after colorectal operation.</td>
</tr>
<tr>
<td>E20</td>
<td>Blood transfusion and increased perioperative risk in coronary artery bypass grafts.</td>
</tr>
<tr>
<td>E21</td>
<td>Frequency and risk factors for subsyndromal delirium in an intensive care unit.</td>
</tr>
<tr>
<td>E22</td>
<td>How current transfusion practices in geriatric patients with hip fracture still differ from current guidelines and the effects on outcome: A retrospective observational study.</td>
</tr>
<tr>
<td>E23</td>
<td>Postoperative acute kidney injury following intraoperative blood product transfusions during cardiac surgery.</td>
</tr>
<tr>
<td>E24</td>
<td>Pre-, Intra-, and Post-Operative Factors for Kidney Injury of Patients Underwent Cardiac Surgery: A Retrospective Cohort Study.</td>
</tr>
<tr>
<td>E26</td>
<td>Delirium following total joint replacement surgery.</td>
</tr>
<tr>
<td>E27</td>
<td>Unrecognized fluid overload during induction therapy increases morbidity in patients with acute promyelocytic leukemia.</td>
</tr>
<tr>
<td>E28</td>
<td>Intra-operative blood transfusion significantly increases the risk of post-operative pulmonary embolism.</td>
</tr>
<tr>
<td>E29</td>
<td>Long length of stay in the ICU associates with a high erythrocyte transfusion rate in critically ill patients.</td>
</tr>
<tr>
<td>E30</td>
<td>Blood Transfusion for Elderly Patients with Hip Fracture: a Nationwide Cohort Study.</td>
</tr>
<tr>
<td>E31</td>
<td>Retrospective Study on Prevalence, Specificity, Sex, and Age Distribution of Alloimmunization in Two General Hospitals in Athens.</td>
</tr>
<tr>
<td>E32</td>
<td>Predictors of Acute Kidney Injury After Hip Fracture in Older Adults.</td>
</tr>
<tr>
<td>E33</td>
<td>The Correlation between Preoperative and Postoperative Hypoalbuminaemia and the Development of Acute Kidney Injury with Respect to the KDIGO Criteria in the Hip Fracture Surgery in Elderly Patients.</td>
</tr>
<tr>
<td>E34</td>
<td>Postoperative delirium in patients with head and neck oral cancer in the West of Scotland.</td>
</tr>
<tr>
<td>E35</td>
<td>Clinical Features and Outcomes of Very Elderly Patients Admitted to the Intensive Care Unit: A Retrospective and Observational Study.</td>
</tr>
<tr>
<td>E36</td>
<td>First annual report of Chinese haemovigilance network.</td>
</tr>
<tr>
<td>E38</td>
<td>Trends in hospitalization, mortality, and timing of colonoscopy in patients with acute lower gastrointestinal bleeding.</td>
</tr>
<tr>
<td>E39</td>
<td>Blood transfusion rates and predictors following geriatric hip fracture surgery.</td>
</tr>
</tbody>
</table>

Source: prepared by the authors.
Twelve types of complications were found in hospitalized elderly people related to age and blood component transfusions. Table 2 presents these, as well as their categorization.

The extracted data were categorized into two areas: surgery-related complications; and non-surgery-related complications. Regarding the first, articles were gathered whose populations had undergone surgery and the complications related to age and blood transfusion happened in the intraoperative or postoperative period. The main procedures described were orthopedic (34.8%), found in articles E2, E6, E9, E10, E14, E16, E17, and E23; cardiac (13%), as explained in E4, E7, and E8; and other surgeries (E12), including colorectal resection (E3) and free flap to reconstruction with oral and maxillofacial surgery (E18).

The data that stood out ranged from longer hospital stay (S2, S6, S14, and S23); postoperative delirium (S3, S9, S10, and S18); postoperative infection (S4, S6, and S23), including sepsis, respiratory wound infection, surgical wound infection, and urinary tract infection; postoperative acute kidney injury (E7, E8, E16, and E17); postoperative acute myocardial infarction (E23); in-hospital mortality (E1, E4, E13, and E14); and postoperative pulmonary embolism (E12). Four (4) articles presented more than one age-related transfusion complication in the hospital setting (E4, E6, E14, and E23).

As for those nonsurgical transfusion complications, two (8.7%) of the articles that associated such complications dealt exclusively with in-hospital mortality (E1 and E13), in addition to the relationship between major TPH and in-hospital mortality (E19 and E22). There was also a relationship between subsidomic delirium (SSD) and hemotransfusion in hospitalized elderly (S5),

Chart 2 – Characterization of the studies according to sample, objective(s) and main results. João Pessoa, PB, Brazil, 2022

<table>
<thead>
<tr>
<th>Art.</th>
<th>Main Results</th>
<th>Observed transfusion complications</th>
<th>Categorization of complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1**</td>
<td>Mortality during hospitalization was higher for transfusion recipients in general; it increased with the number of units given and with patient age, being higher in the extremes (&lt;1 year; &gt;70 years) for any type of blood component.</td>
<td>* Higher in-hospital mortality</td>
<td>Non-surgical complications</td>
</tr>
<tr>
<td>E2**</td>
<td>Advanced age and need for blood transfusion were two predictors of longer hospital stays after primary total knee arthroplasty.</td>
<td>higher *TPH</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E3**</td>
<td>10% of patients operated on for colorectal cancer developed DPO; advanced age, history of psychiatric illness, and perioperative transfusion were stronger independent risk factors for DPO.</td>
<td>*DPO</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E4**</td>
<td>Patients ≥ 75 years old undergoing blood transfusions had a significantly more prevalent composite infectious outcome; three times higher risk of death.</td>
<td>*Infection&lt;br&gt;*Higher hospital mortality</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E5**</td>
<td>Advanced age and transfusion were risk factors highly associated with subsidomic delirium symptoms.</td>
<td>*DPO</td>
<td>Non-surgical complications</td>
</tr>
<tr>
<td>E6**</td>
<td>Transfused patients had longer hospital stays and a higher odds ratio of contracting infection, regardless of whether the transfusion was liberal or restrictive.</td>
<td>*TPH major&lt;br&gt;*Infection</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E7**</td>
<td>Advanced age was one of the variables associated with worsening LRA; association between RBC transfusion and development of LRA; association of fresh frozen plasma and platelet transfusion with the development of LRA in cardia surgery.</td>
<td>*Post-surgical LRA</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E8**</td>
<td>Older age and transfused RBCs identified as independent risk factors for LRA after cardiac surgery.</td>
<td>*LRA post-surgical</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E9**</td>
<td>1–8% of the sample developed DPO; receiving intraoperative blood transfusion was a risk factor for postoperative delirium, regardless of anemia status on admission.</td>
<td>*DPO</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E10**</td>
<td>Older age and hemotransfusions identified as risk factors for DPO.</td>
<td>*DPO</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E11**</td>
<td>High total volume of transfusions and advanced age as factors associated with fluid overload during induction.</td>
<td>*Water overload</td>
<td>Non-surgical complications</td>
</tr>
<tr>
<td>E12**</td>
<td>Intraoperative blood transfusion as a significant predictor for EP after surgery, as well as advanced age.</td>
<td>*EP in the post-operative period</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E13**</td>
<td>As for ICU mortality, age and ≥5 units transfused were predictors of mortality.</td>
<td>*Higher in-hospital mortality</td>
<td>Non-surgical complications</td>
</tr>
<tr>
<td>E14**</td>
<td>The average hospital stay in the transfusion group was significantly longer, with more risk of all-cause mortality.</td>
<td>*Higher TPH&lt;br&gt;*Higher in-hospital mortality</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E15**</td>
<td>The mean age of patients in whom an alloantibody was identified was 67.99±17.56 years (mostly in the age range of 71 to 80 years); patients with multiple antibodies were older compared to patients with a single antibody.</td>
<td>*Aloimmunization</td>
<td>Non-surgical complications</td>
</tr>
<tr>
<td>E16**</td>
<td>The age of patients who developed LRA was significantly higher; postoperative blood transfusion was associated with increased risk of LRA.</td>
<td>*LRA post-surgical</td>
<td>Surgical complications</td>
</tr>
<tr>
<td>E17**</td>
<td>Advanced age and transfusion of blood products during the operation were significantly associated with the development of LRA.</td>
<td>*LRA post-surgical</td>
<td>Surgical complications</td>
</tr>
</tbody>
</table>
as well as presentation of transfusion reactions most often found in this group (S11, S15, S20 and S21).

In general, this study points out that blood transfusion in the elderly hospitalized patients acts as a potential risk factor for the development of complications beyond those known to be attributed to blood products (transfusion reactions), often being a factor subject to modification.

**DISCUSSION**

The studies’ results identified that blood transfusion alone may act on the development of complications in hospitalized elderly patients, recognizing at least 12 types of adverse effects. Add to that the fact that transfused patients usually present more severe ICU conditions, have lower hemoglobin levels, and stay longer in the ICU, with a higher mortality rate than non-transfused patients, as pointed out by E13.29 According to this study, the number of packed red blood cells units transfused is a predictor of mortality, along with age and organ support therapies, and may be considered a sign of severity and responsible for increased mortality and severe complications.

Thus, patients who received frequent transfusions were thought to be sicker than those who did not. Therefore, they are more likely to have death as the outcome.17

With regard to increased mortality and TPH among elderly hemotransfused patients, findings38 reiterate that the impact of age and comorbidities on risk stratification for this population is too high. However, E4 counters such information by stating that despite the fact that hemotransfused patients have higher surgical risk, when only low-risk patients were selected, mortality still remained high.28

For the elderly who receive transfusion due to surgical procedures, the literature found that those who received RBCs do not show significant postoperative improvements in relation to decreased TPH and mortality.39 Similarly, S2 and S19 associated hemotransfusion with increased risk of death and TPH, highlighting that the pre-existence of comorbidities as well as decreased physiological reserves during older age negatively affect prognosis.18,35

In this guideline, transfusion was also associated with increased risk of urinary tract infection (UTI) and acute myocardial infarction (AMI).39 The procedure has been shown to be immunosuppressive, decreasing immune responses to infection. Moreover, allogeneic RBCs from a donor could cause amplification of circulating antigens, resulting in immune fragility. Factors such as surgery time and administration of erythropoietin and iron can prevent the development of anemia and blood loss, with consequent reduction in the need for transfusion, preserving from complications arising from hemotransfusion.

The impact of the procedure also reveals itself in mental activity. Studies have found that advanced age and transfusion are independent risk factors for the development of postoperative delirium (POD).19,34 One of the reasons for such a reaction occurs due to decreased oxygenation of the brain during surgery. However, cytokines, which have an active role in this process by causing an inflammatory cascade, said to be responsible for acute episodes of delirium, may also explain POD.35

Faced with the decline of cognitive abilities, which in themselves already contribute to POD in the elderly, the healthcare team must act with greater sensitivity. The help for the patient to know how to deal with possible mental confusion experienced and to understand his momentary reality is fundamental.31

Another frequent factor in the observation of these geriatric patients was acute kidney injury (AKI). Research states that people with advanced age would have impaired blood pressure autoregulation, which would cause impaired renal function (RF).21,24,32 These findings reinforce the hypothesis that perioperative hypotension is the main cause of AKI in this public, also exposing that the link between blood transfusion and AKI is probably the manifestation of preexisting acute disease and not a direct causality of AKI by the transfusion itself. The high prevalence of malnutrition among elderly patients was also associated with
AKI by E17, exposing that low albumin levels would enable its occurrence, since this exerts a protective effect on RF.\(^3\) For gerontes who received transfusion but did not undergo surgical processes, the literature found that transfusion reactions can also occur frequently. In these cases, pre-existing risk factors act negatively on the picture, contributing to the occurrence of the adverse events. Elucidatively, older patients with transfusion-associated circulatory overload (TACO) tend to have a history of hematologic malignancies, congestive heart failure, and/or coronary heart disease.\(^4\)

Furthermore, in the case of transfusion-related acute lung injury (TRALI), it has been detected through research that its diagnosis has occurred in the 65 – to 79-year age group, especially in the elderly with acute kidney disease and liver failure.\(^5\) Although TRALI is rare, it can be fatal. It develops within a period of up to 6 hours after the procedure, and is also related to the existence of donor-specific antibodies that attack the pulmonary endothelium.\(^6\)

An interesting fact was seen in S15, which detected a high percentage of hemotransfused patients with multiple anti-erythrocyte antibodies (allo and autoantibodies). Alloimmunization ends up affecting organisms in many ways, leaving the transfusion process highly complex, since its development is associated with increased risk of acute and late hemolytic reactions after transfusion, in addition to cross-incompatibility, which impacts blood availability in urgent medical situations.\(^5\) Considering that chronic diseases, such as oncological and/or hematological ones, require multiple transfusions, this is a worrisome factor that deserves attention.

The increased risk of pulmonary embolism in hemotransfused elderly has also been noted.\(^7\) This mechanism can be explained by the potential of transfused blood to cause an imbalance in coagulation factors, modulating the inflammatory cascade. The storage time of red blood cells may be associated with their greater aggregation, making their interaction with the endothelium more difficult. Thus, oxidative stress would contribute to the formation of microparticles and hemolysis of the cells, with association to venous thrombosis and, consequently, pulmonary embolism.

Thus, it can be noticed that, according to the selected studies, elderly patients have comorbidities that alter their physiological reserves and their ability to react to stressors. In the meantime, blood transfusion is able to cause immunosuppressive and inflammatory reactions in human organisms, and may cause complications due to reactions resulting from it. Therefore, studies recommend caution and the adoption of a restrictive blood transfusion strategy for critically ill patients, being indicated only when it is essential to life.

**CONCLUSION**

The scientific literature on transfusion complications in hospitalized elderly has found a relationship with age, clinical conditions and adverse reactions, which eventually generate such complications, indicating the need for productions that enhance care to the transfused elderly. It is known that the high inflammatory and immunosuppressive capacity of blood transfusion, combined with the inherent characteristics of human aging, may result in the injuries exposed by this study.

Although most publications have identified the adverse effects related to blood transfusion in hospitalized elderly already exposed, the mechanisms that predispose to them are not fully understood. In order to better evidence them, it is necessary to perform more prospective, clinical and/or experimental studies, although it is understood that the risks involving such studies may be responsible for the scarcity of those with a clinical and/or experimental approach.

Furthermore, one cannot deny the benefits of blood transfusion for the recovery of homeostasis of the organism that needs it. However, just as it can be beneficial, it can also have consequences, including fatal ones. The healthcare team must consider that the therapeutic use of blood must be done with caution, evaluating whether the benefits will be greater than the harm.

Facing this reality, it is up to the nurse and his team the responsibility and commitment with the continuous care to the hemotransfused elderly person, once they remain most of the time by the patient’s side during his hospital stay. The early identification of signs of adverse events should not be overlooked, and permanent education in the services is suggested for the knowledge of professionals on the subject.

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