Among the absolute changes between baseline and follow-up, we found only a significant difference between the groups for creatinine clearance \((P < 0.01)\), whereas u-NGAL, u-NGAL\(_{CR}\) (urinary neutrophil gelatinase-associated lipocalin adjusted for creatinine), and urine output did not deviate significantly. Among the relative changes, calculated as (follow-up - baseline)/follow-up x 100, only creatinine clearance deviated significantly \((P = 0.02)\), whereas no significant differences were found in u-NGAL, u-NGAL\(_{CR}\), and urine output. Thus, creatinine clearance increased slightly in the HES group and was unchanged in the saline group.

**Competing Interests**
The authors declare no competing interests.

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**References**


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used in previous studies during loss and recovery of consciousness because of anesthetics\textsuperscript{3,6} and in vegetative state.\textsuperscript{7} Therefore, these findings may be considered as more reliable, especially where the study of Khodayari-Rostamabad \textit{et al.} reports conflicting results.

Calculating the characteristic path length and clustering coefficient provides information on the topology of the underlying functional network. Khodayari-Rostamabad \textit{et al.} used weighted graph analysis to compare differences in path length and clustering coefficient between remifentanil and placebo. In a weighted graph, the functional connectivity strength is used to weigh the connection between any two nodes in the network. These weights of the connections have a direct influence on the network characteristics, \textit{i.e.}, clustering coefficient and path length.\textsuperscript{8} When the functional connectivity strength is increased, the path length will reduce and clustering coefficient will increase automatically. As the authors found a lower functional connectivity strength during remifentanil infusion \textit{versus} placebo, this may at least partly explain the higher path length and lower clustering coefficient during remifentanil infusion.

A commonly used correction procedure for network analysis based on a weighted graph is normalization of network measures. Normalized measures can be obtained by dividing the path length and clustering coefficient by the characteristics of simulated random networks with the same connection density and strength. However, this normalization does not solve the bias completely.\textsuperscript{9} A recently introduced method to evaluate the underlying functional network is the minimum spanning tree, which may solve the need for normalization.\textsuperscript{9} The minimum spanning tree is an acyclic subgraph in which the most important connections are included. This results in a mathematically defined subnetwork with a fixed density and degree, which may be more appropriate for group comparisons of network topology, and increase comparability between different studies.\textsuperscript{10}

Studies exploring the effects of anesthesia using functional connectivity and network analysis are important to increase our understanding of the complex phenomena such as consciousness. Recent work provided an interesting view of the underlying mechanism of anesthetics. Unconsciousness induced by propofol results in reconfiguration of the network by a shift of the primary hub (\textit{e.g.}, the highest connected node) from the parietal to the frontal lobe.\textsuperscript{5} Furthermore, in healthy subjects, a change of directionality of the functional connectivity was found during anesthesia-induced loss of consciousness, which normalized after consciousness was regained.\textsuperscript{11–13}

In conclusion, the work by Khodayari-Rostamabad \textit{et al.} should be interpreted with caution because of the methodological limitations described earlier. As long as the field connectivity analysis is evolving rapidly and analysis techniques are constantly being optimized, it is important to use state-of-the-art methodology when studying functional brain networks in a clinical setting.

\textbf{Competing Interests}

The authors declare no competing interests.

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