

Author: Tom Latham

With contributions from the SHOT Pulmonary Working Expert Group members

Pulmonary complications remain the largest category contributing to transfusion-associated deaths reported to SHOT and the second most common category of transfusion reactions. Patients with respiratory complications are often elderly with multiple co-morbidities which could all contribute to issues post transfusion. These complications present diagnostic and therapeutic challenges with mainly supportive measures available and specific therapies are lacking.

At least some of these pulmonary complications are potentially preventable and early recognition with prompt treatment is vital. Patient education and awareness are also important, especially if transfused as day cases or in the community.

Blood components should only be administered after careful consideration of the patient's unique risk of a transfusion complication versus the physiologic benefit of the planned transfused blood component. Less is often more with regards to transfusion.

A significant intervention in 2024 involved the issuing of a National Patient Safety Alert (NatPSA) in the UK to address the rising numbers of pulmonary complications (MHRA and SHOT, 2024). To our knowledge this is the first systematic attempt to address the prevention of pulmonary complications on a national scale. NatPSA/2024/004/MHRA was issued on 4 April 2024 via the NatPSA system, following extensive review. A target date of October 2024 was given to complete the comprehensive set of recommendations. The recommendations have all been existing SHOT recommendations for several years. The alert did appear to achieve a high level of engagement within the transfusion community, given the good attendance at webinars conducted by SHOT and constructive queries received from transfusion teams.

The total number of pulmonary complications continues to increase: The existing trend of increasing reports of transfusion-associated circulatory overload (TACO) continues, with a marked increase in reports received in 2024. A greater proportion of the reported TACO cases in 2024 were thought to be of imputability 2 or higher, than in previous years. The number of non-TACO complications has also increased; the majority of these were also thought to be predominantly due to fluid overload based on a compelling clinical scenario, although they did not meet TACO criteria. It is unclear whether any effect of the NatPSA on prevention may have been offset by an increase in reporting because of improved awareness. However, the hallmark signal of an effective safety system (increased reporting but decreasing severity of outcomes) is not seen here yet, as deaths have also increased.

Data from cases reported to SHOT this year provide early indicators of the uptake and effectiveness of the NatPSA recommendations: Use of the TACO pre-transfusion risk assessment is the most explicitly measurable intervention, as this is an existing question in the dataset collected for all suspected pulmonary complication reports to SHOT.

There appeared to be better use of the TACO pre-transfusion risk assessment in 2024 compared to previous years: Where data was supplied, the TACO pre-transfusion risk assessment was completed in 29/49 (59.2%) reports, where the incident occurred after the October completion date. This is an improvement on the historical rate, which had plateaued at around a third of cases (Narayan, et al., 2024) but not significantly different to the completion date for incidents occurring prior to the April issue date of the alert, 29/50 (58.0%). It is too early to determine the long-term effects of the NatPSA.

Fluid risks were common, but suboptimal application of the tool may have limited its effectiveness in identifying the risk: A fluid risk was retrospectively identified in 112/122 (91.8%) evaluable cases submitted, using the criteria in the SHOT risk assessment. There was a statistically significant association ($p=0.02$ using Fisher exact test) between a risk factor being identified during risk assessment and a fluid overload risk factor being identified retrospectively, but only 60/112 (53.6%) cases where a fluid risk was present were identified on prospective risk assessment.

Excessive and unnecessary transfusion occurred in many TACO cases: Evidence of excessive or unnecessary transfusion was present in 46/188 (24.5%) TACO cases. Excessive transfusion is an avoidable factor both for TACO and non-TACO complications. There should be a systematic approach to the decision to transfuse, considering the cause of anaemia and risks/benefits of transfusion which then informs the appropriate dose of red cells.

Appropriate use of the pre-transfusion risk assessment tool appears effective at prompting recommendations for mitigating actions, but there is variability in the range of actions proposed:

Reported data indicates that at least one mitigating action was recommended in 85/95 (89.5%) cases where a fluid risk was identified on risk assessment. Where mitigating actions were recommended, this included a diuretic in 32/60 (53.3%) evaluable cases. These appear to show improvement compared to the 2017 National Comparative Audit, where diuretic was prescribed in only 11% of patients at risk of fluid overload (TACO Audit Working Group on behalf of the NCABT, 2018). The available data is not able to demonstrate how practices such as 'close monitoring' would have differed from practice if the risk assessment had not been performed.

Substantial numbers of reactions due to fluid overload occurred despite mitigating actions:

Including both TACO cases and non-TACO cases where the working group considered fluid overload was likely to have contributed to the reaction, 57/193 (29.5%) had at least one mitigating action recommended, and 29 had received prophylactic diuretic (15.0%). In other words, about 1/3 of TACO cases occurred despite full use of the preventive measures recommended

There is a high rate of suspicion of fluid overload post reaction: Diuretics were given at the time of reaction in 178/193 (92.2%) evaluable cases considered to be due to fluid overload. This does appear to suggest improvement compared to the National Comparative Audit in 2017, where diuretic use was 76% (TACO Audit Working Group on behalf of the NCABT, 2018). The SHOT TACO investigation guidance tool was reported as being used retrospectively in 121/222 (54.5%) evaluable cases overall.

In summary, it has not been possible to demonstrate any early and measurable effect of the NatPSA on pulmonary complications following transfusion: There is some evidence of gradual improvements in the use of TACO prevention measures and the recognition and treatment of TACO, but this has not translated into a reduction in cases or deaths. A UK-wide survey is being planned at the end of 2025 to understand challenges in implementation of the recommendations from the NatPSA. Monitoring will continue and there will be further scope for implementation to gain ground with completion of local audit and improvement cycles, even after the target completion date.

Incomplete implementation and incomplete effectiveness of interventions may both contribute to residual risk:

Interpretation of the reasons for a lack of response to the intervention are constrained by a lack of control data; we do not know whether the increase in cases is due to increasing numbers of cases at risk or increased reporting. It is also not clear as to how many cases might have occurred were it not for the intervention. The data does show that the use of the TACO pre-transfusion risk assessment is still far from universal. What more could be done to improve usage rates? Managerial approaches to improving transfusion safety practices, such as benchmarking performance indicators between hospitals, have been proposed and are indeed likely to improve uptake. Without addressing the root causes of why it appears difficult in practice to perform and document risk assessments, there is a danger that simply enforcing compliance may not actually improve the quality of risk identification.

Investigating why risks of fluid overload are not always identified when applying the TACO risk assessment tool will also help improve effectiveness of the tool. There is an unmet need to identify the most appropriate interventions when the risk of fluid overload is present, since many cases of TACO occur despite mitigation actions being performed. Improvements might include more specific guidance on the use of diuretics and monitoring of the response to diuretics. However, there is almost no clinical trial evidence to inform these recommendations. Clinical trials of TACO-prevention interventions must be considered a priority for transfusion medicine, but previous attempts to conduct trials have proved problematic (Pendergrast, et al., 2019). Data from haemovigilance systems should inform clinical research priorities. Haemovigilance organisations could perhaps have a stronger role in influencing these priorities so that research questions address the most common causes of clinical harm.