USING AN EMBEDDED IMPLEMENTATION FRAMEWORK IN A PILOT TRIAL OF PRONE POSITIONING FOR NON-INTUBATED HYPOXIC ADULTS WITH COVID-19

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BACKGROUND

- Prone positioning is an appealing therapeutic strategy for non-intubated hypoxic patients with COVID-19 but its effectiveness remains to be established in randomized controlled trials.
- The awake prone strategy is a complex medical intervention, with multiple implementation nuances such as adoption, feasibility, and tolerability that may affect successful conduct of an informative RCT

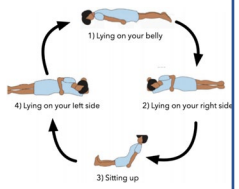
OBJECTIVE: To identify contextual factors relevant to the conduct of a informative RCT evaluating prone positioning for non-intubated hypoxic patients with COVID-19

METHODS

- Study Overview: Pilot trial with implementation outcome framework
- Design: Two-arm, pragmatic, cluster-randomized pilot trial with embedded implementation evaluation
- Setting: A tertiary care teaching hospital in Charlotte, North Carolina
- Patients: 40 adults with COVID-19 and hypoxia who were not yet intubated
- Comparison: Usual care (UC; i.e., routine COVID-19 therapy and respiratory support), vs added APPS strategy (Fig 1)
- Main Outcomes: Acceptability, adoption, appropriateness, effectiveness, equity, feasibility, fidelity, and penetration

Figure 1: Graphic guide to the Awake Positioning Strategy.

Key considerations for the Awake Prone Positioning Strategy
- Maintain prone position as long as possible
- Use pillows or other support to optimize comfort and tolerability
- Be mindful of discomfort due to pressure and adjust as needed



RESULTS

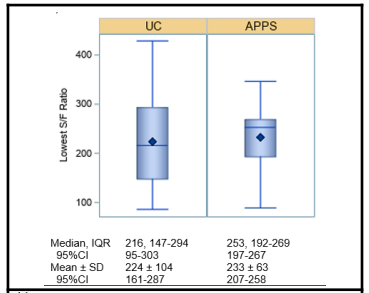
- Mixed methods analyses uncovered several barriers relevant to the conduct of a successful definitive RCT, including low adherence to prone positioning, large differences between physician-recommended and patient-tolerated prone durations, and diffusion of prone positioning into usual care (Table 1)

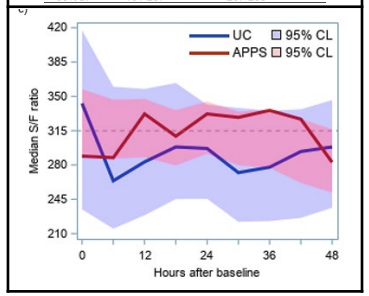
- Oxygenation outcomes are shown in Fig 2. Patients in the Usual Care group (n=13) had a median nadir S/F ratio over the 48-hour study period of 216 [95%CI=95-303] versus 253 [95%CI=197-267] in the APPS group (n=27). Patients in the Usual Care group spent 42 hours [95%CI=13-47] of the 48-hour study period below S/F ratio < 315 versus 20 hours [95%CI=6-39]) for patients in the APPS group.

Table 1: Results and implications of convergent mixed methods analysis presented using implementation outcome framework with associated implications for a future RCT

Outcome	Quantitative Results	Qualitative Results	Implication for future RCT
Acceptability of an RCT evaluating APPS	57% of clinicians perceive randomization to control group unacceptable	Clinicians report perceived lack of equipoise for prone positioning, lack of alternatives	May hinder recruitment or lead to selection bias; consider clinician education strategy or switch to non-traditional (e.g. quasi-experimental) trial design
Adoption of an RCT evaluating APPS	74% of physicians assigned to APPS prescribed the intervention to eligible patients		May require modifying intervention to encourage uptake, anticipate dilution of treatment effect in intention-to-treat analyses
Appropriateness of an RCT evaluating APPS	71% of clinicians reported that trial intervention has become usual care		Consider organizational education strategy to reinforce equipoise or quasi-experimental design
Effectiveness of an RCT evaluating APPS	Direction of research outcomes favored prone positioning 100% of respondents endorsed ICU utilization and/or advanced respiratory support rates to be relevant and patient-centered primary outcome	Patients subjectively felt that prone positioning improved their breathing	Further investigation of prone positioning for non-intubated patients in larger studies likely warranted; potential patient centered outcomes might include ICU or advanced respiratory support utilization
Equity of an RCT evaluating APPS	Lower rates of adherence among Black (19%) compared to white (56%) and non-Black Hispanic (71%) patients		Develop culturally tailored approaches to reduce disparities in adherence
Feasibility of an RCT evaluating APPS	98% of patients completed the study Only 2 of 27 patients had documentation of prone position duration Outcome data collection: no missing data for ICU transfer, advanced respiratory support, or mortality	Nurses reported adherence to a strict positioning schedule to be challenging due to complexities of care environment	Tailor strategies to reduce complexity and increase flexibility of the intervention delivery protocol Traditional RCTs with active data collection or novel approaches such as smart phone applications and patient-reported measures will be needed if reliable estimates of prone duration are desired. Otherwise, pragmatic trials should not plan specific analyses around these data
Fidelity of an RCT evaluating APPS	50% of patients had protocol violations/crossovers 0% of patients managed the 12-16 hours prone target time suggested by clinicians.	Patients perceived prone positioning to be difficult	Will require strategies to enhance organizational and individual buy-in and improve comfort/tolerability Anticipate dilution of treatment effect, plan education strategy to clinicians to limit crossovers
Penetration of an RCT evaluating APPS	No patients experienced intubation or death during hospitalization		Adapt recruitment strategies, may require inclusion of non-intubated patients admitted to ICU

Figure 2: Separation of lowest S/F ratio and trends in median S/F ratio





CONCLUSIONS

Several barriers to conducting a trial of the effect of prone positioning in non-intubated patients with COVID-19 need to be addressed to ensure yield of informative results that will be readily translated into practice.