Introduction
Fistulas continue to be promoted as the vascular access of choice due to their lower complication rates as compared with catheters (1,2). However, depending on the fistula cannulation method, the infection risk can compared with that of a catheter. Traditionally, cannulation is an area most physicians tend to ignore; instead, the choice and technique of cannulation is routinely left to nurses. However, given the pain, fear, and anxiety with cannulation that most hemodialysis patients experience (3–5), all health care providers should pay more attention to needling. Furthermore, cannulation and its associated mishaps can lead to fistula complications of infection, and decreased patency.

The most common method of cannulation among maintenance hemodialysis patients is the rope ladder technique, which rotates needling sites along the full length of the fistula. The area wall technique, where favored regions are repeatedly needled, is actively discouraged due to progressive weakness in the vessel wall and subsequent aneurysm formation (6). Buttonhole cannulation is more often used in home hemodialysis and it was first introduced as a measure to cannulate a fistula with a limited area for needling (7). Buttonhole involves a constant site of needling that, over time, leads to an epithelized track into which a blunt needle is inserted. Since its first introduction almost 50 years ago by Dr Twardoski and his head nurse (Sister Kumara), buttonhole has continued to garner widespread enthusiasm. Support for its use has been mostly promoted by observational data and poor-quality methodology studies showing beneficial effects on pain and fewer needling complications. Nephrology societies (8,9) (renal.org/guidelines) still recommend buttonhole use as a means to reduce pain and increase longevity.

In order to promote a novel cannulation technique over the standard of care, there should be evidence of benefit and a lack of demonstrable harm. Buttonhole cannulation lacks evidence to support a consistent benefit and, distressingly, is associated with potential harm, as reviewed in the paragraphs below.

Evidence Does not Support a Reduction in Pain with Buttonhole Cannulation
Supporters of buttonhole refer to multiple studies (6,7) and a meta-analysis of observational studies showing significant reduction in pain (10). The concern with these studies is that they are limited by selection bias and residual confounders. The best-quality evidence regarding buttonhole cannulation comes from five randomized trials (11–15), and when these studies are included in the meta-analysis there is no signal of reduced pain (10). Four of the five randomized trials showed no improvement in pain with buttonhole cannulation. The only randomized trial (14) to report “less pain with needling” did not actually report on the magnitude of effect, nor describe how this outcome was measured, making this result questionable. In both our study (12) and the trail by Vaux et al. (15), there was a trend to worse pain with buttonhole. A larger proportion of patients had a high pain score with buttonhole as compared with rope ladder cannulation (12), and more patients withdrew from buttonhole cannulation (15) due to pain. In summary, the literature does not support the idea of improved pain with buttonhole needling among in-center hemodialysis patients (Table1).

Buttonhole Might Reduce Hematoma and Aneurysm Growth but the Effect on Access Survival Is Unclear
Observational studies report fewer needling complications (17) of infiltration and hematoma (16), improvements in aneurysm size (18), and better time to hemostasis (6,17,18,20). Two randomized trials demonstrate fewer hematomas (12,13): 295 per 1000 dialysis days for buttonhole versus 426 per 1000 dialysis days for rope ladder needling in our trial. A third trial (11) showed an increase in hematomas with buttonhole, whereas the remaining two randomized trials did not report on this, giving an overall unclear effect on hematoma. The shorter time to achieve hemostasis seen with buttonhole in observational studies is not substantiated by randomized data, in which all five studies found no difference in hemostasis after needle removal. The improvement in aneurysm size noted in observational studies was also seen in two of the randomized trials (but not reported in the other three). Struthers et al. (13) noted an increase in the size of fistula diameter of 30% in rope ladder versus only 1% in buttonhole. Vaux et al. (15) also showed less growth
of the fistula diameter with buttonhole (23%) as compared to rope ladder (67%).

If, in fact, buttonhole cannulation leads to fewer hematomas and less aneurysmal growth of the fistula, this might translate into fewer access interventions and longer access survival. The need to maintain a well functioning access is paramount for hemodialysis patients. Most patients who have a fistula can expect 2.75 access procedures/year (28). Access procedures are a high burden for patients, which effect their quality of life. Unfortunately, the effect of buttonhole cannulation on access interventions has conflicting results in observational studies (19,20,22). One showed fewer interventions with buttonhole (22) compared with the rope ladder method; however, the control group was from a different hemodialysis unit, making it difficult to draw conclusions. Another observational study showed no improvement in fistula patency and a trend to more interventions with buttonhole cannulation ($P = 0.07$) (19).

The evidence from randomized trials shows conflicting results. Vaux et al. (15) showed a reduced number of interventions in buttonhole (0.4 versus 0.2 interventions/patient per year with buttonhole). However, many of the patients randomized to buttonhole (14 of 58) switched to rope ladder cannulation but were analyzed as buttonhole, which likely affects interpretation. Contrary to their conclusions, we found, in an intention-to-treat analysis (21), an increase in the number of procedures and interventions on buttonhole patients, and no difference in access survival. One main difference between these two studies was the use of a polycarbonate peg to promote buttonhole track formation (Vaux et al. (15)) instead of repeated cannulation at a constant site (15) using a sharp needle (MacRae et al. (21)). Peg creation of buttonhole might lead to fewer false tracks and less mechanical injury to the vessel wall, which might affect the risk of fistula stenosis (29) and lead to more favorable outcomes. Over time, regardless of technique, cannulation leads to intimal hyperplasia and the development of stenosis. Buttonhole cannulation has been shown to have endothelial hyperplasia at the sites of cannulation (30), which may lead to stenosis formation (31). Clearly more study is required to determine if the technique of cannulation is in fact an important determinant of fistula patency and survival.

### The Risk of Infection with Buttonhole Is Exceedingly High

Any potential benefit of buttonhole cannulation must be weighed against the most concerning effect: that of increased infection (Figure 1). A recent meta-analysis (10) of observational and randomized trials of buttonhole cannulation showed a very high risk of infection with an odds ratio 3.19 [95% confidence interval (CI), 2.12 to 4.77]. A recent review (27) of bacteremia in 882 hemodialysis patients from a program that had buttonhole cannulation as standard of care showed that the risk of *Staphylococcus aureus* bacteremia with buttonhole cannulation, hazard ratio (HR) 3.6 (95% CI, 1.4 to 9.5), approaches that of patients with catheters, HR 5.3 (95% CI, 1.9 to 18.6). These high rates of bacteremia prompted the hemodialysis program to introduce a variety of measures designed to reduce infection rates, such as restricting the number of buttonhole cannulators, introducing an intensive asepsis policy, and avoiding buttonhole use among patients who were nasal carriers of *S. aureus*. These measures, which were initially successful in reducing infections, were followed by a subsequent relapse.

Our own experience with buttonhole is that it is associated with significantly more *S. aureus* bacteremia than standard cannulation. Similar to Labriola et al. (25), we have also

| Table 1. Summary of buttonhole cannulation outcomes |
|----------------|----------------|----------------|
| Outcome        | Increased Effect | Decreased Effect | No Effect |
| Pain           | MacRae et al. (12)$^a$ | Twardoski et al. (7) | Struthers et al. (13)$^a$ |
|                | Vaux et al. (15)$^a$  | Toma et al. (14) | Chow et al. (11)$^a$ |
| Hematoma       | Chow et al. (11)$^a$  | Struthers et al. (13)$^a$ | MacRae et al. (12)$^a$ |
|                |                      | Pergolotti et al. (16) | Kim et al. (17) |
| Aneurysm       | Chan et al. (19)    | Marticorena et al. (18) | Struthers et al. (13)$^a$ |
|                | MacRae et al. (21)$^a$ | Vaux et al. (15)$^a$ | Vaux et al. (15)$^a$ |
| Fistula procedure | Nesrallah et al. (23) | Ludlow et al. (20) | Van Loon et al. (22) |
|                | Struthers et al. (13)$^a$ | Vaux et al. (15)$^a$ | Vaux et al. (15)$^a$ |
|                | Van Eps et al. (24) |                      |             |
|                | Chow et al. (11)$^a$  |                      |             |
|                | Labriola et al. (25) |                      |             |
|                | MacRae et al. (12)$^a$ |                      |             |
|                | Vaux et al. (15)$^a$  |                      |             |
|                | Muir et al. (26)     |                      |             |
|                | Collier et al. (27)  |                      |             |

$^a$Randomized trials.
noted that the onset of bacteremia is delayed, with a median time to infection of 11 months. Thus, studies of short duration will underestimate the risk of infection associated with this technique. All of the randomized buttonhole studies, including that by Vaux et al. (15), have shown an increase in the number of localized infections. Whereas we noted significantly more *S. aureus* bacteremia with buttonhole, Vaux et al. did not see increased bacteremia. There are a couple of differences between these studies that are worth highlighting. The use of polycarbonate pegs to create the track and the use of face masks during buttonhole cannulation may have reduced the risk of infection.

**Potential Mechanisms of Infection in Buttonhole**

*S. aureus* colonization of the nares with subsequent transmission to the buttonhole scab site may promote the introduction of bacteria into the buttonhole track, which acts as a nidus for infection. Toma et al. (32) obtained sterile culture samples from the buttonhole track in 59 patients, and found *S. aureus* in 5.1% and *Staphylococcus epidermis* in 13.6% of the tracks. Another study of prospectively tracked bacterial cultures from the buttonhole scab and insertion sites among 84 patients revealed a 20% culture positive rate (33). Colonization of the buttonhole tracks with *S. aureus* and *S. epidermis* was associated with more access-related infections than those with negative cultures or mixed organisms.

Autopsy studies indicate that buttonhole tracks develop granulated tissue in response to repeated contact of the needle along the track (34). Over time, the granulated tissue manifests either as a deformity at the surface of the buttonhole site or as a narrowing within the vessel lumen. The deformity makes it harder to remove fragments of the scab, which promotes bacterial migration from the skin into the track, thus, promoting bacterial colonization (34). False buttonhole tracks, created when multiple cannulators are involved, can also lead to increased risk of infection (35), potentially by the mechanism above. Nurses perceive buttonhole cannulation as harder than routine cannulation (12), and with multiple cannulators there are likely many false tracks. The polycarbonate peg method of buttonhole formation might lead to a lower risk of infection by reducing the number of false tracks. However, polycarbonate pegs, which are potentially useful for track creation, are limited in their widespread use by high cost.

**Buttonhole Outcomes Are not Any Better in Home Dialysis Patients**

The increased risk of infection associated with buttonhole cannulation for in-center hemodialysis patients is also a concern for those who dialyze at home (23). In an observational cohort of home hemodialysis patients, there was a significant increase in infections with buttonhole cannulation as compared with rope ladder cannulation (0.4/1000 days versus 0.1/1000 fistula days (26)). Despite implementation of preventative measures such as topical mupirocin (23), re-education on asepsis measures and audits of technique, the risk of bacteremia remains high (24,26). Routine audits of technique in home hemodialysis patients (36) show that buttonhole cannulation leads to more errors than either rope ladder cannulation (P<0.037% versus 37%, P=0.008) or use of a catheter (P=0.01). Errors with buttonhole cannulation are related to inappropriate scab removal and poor aseptic technique, which, over time, may contribute to the increased bacteremia rates. Health care providers, including nephrologists, need to be aware that pain and fear associated with needling is a major area of concern for patients (3,4). Anxiety and the uncertainty surrounding fistula cannulation are highlighted in qualitative studies (5). Clearly, cannulation techniques, and their risks and benefits, should be part of vascular access education for patients and health care providers. Physicians need to be more engaged in the cannulation process, and need to be aware of the benefits and risks in order to promote shared decision making with patients. The current evidence supports fewer hematomas, unclear impact on fistula survival, similar reports of pain, and very high infection rates with buttonhole cannulation. Concerningly, the infection risk with buttonhole persists even with the use of prophylactic strategies such as topical mupirocin and frequent review of technique. Infection with *S. aureus*, as a consequence of buttonhole cannulation, has high septic complication (22.6%) and mortality (9.7% at 30 days) rates (27).

Due to the high risk of infection associated with buttonhole, this method of cannulation should not be promoted, and yet health care providers continue to do so. If we are to apply the principles of evidence-based medicine, then the judicial use of the current best evidence suggests that rope ladder cannulation is the cannulation of choice hemodialysis patients.

**Author Contributions**

J MacRae conceptualized the study, wrote the original draft, and was responsible for reviewing and editing the manuscript.

**Disclosures**

J. MacRae has nothing to disclose.

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**References**


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