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**Finding a Solution:
Heparinised saline versus normal saline in the maintenance
of invasive arterial lines in intensive care**

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Keywords:	Arterial line, Heparin, Monitoring, Patient safety
Abstract:	<p>Background We assessed the impact of heparinised saline (HS) versus 0.9% normal saline (NS) on arterial line patency. Maintaining the patency of arterial lines is essential for obtaining accurate physiological measurements, enabling blood sampling and minimising line replacement. Use of HS is associated with risks such as thrombocytopenia, haemorrhage and mis-selection^{1,2}. Historical studies draw variable conclusions but suggest that NS is at least as effective at maintaining line patency, although recent evidence has questioned this³.</p> <p>Methods We conducted a prospective analysis of the use of HS versus NS on unselected patients in the intensive care of our hospital. Data concerning duration of 471 lines insertion and reason for removal was collected.</p> <p>Results We found a higher risk of blockage for lines flushed with NS compared with HS (RR= 2.15, 95% CI 1.392 to 3.32, P=< 0.001). Of the 56 lines which blocked initially (19 HS and 37 NS lines), 26 were replaced with new lines. Eight heparinised lines were replaced and 18 NS lines. Five of these replaced lines subsequently blocked again, all of which were heparinised lines.</p> <p>Conclusions Our study demonstrates a significantly important reduction in arterial line longevity when flushed with NS compared to HS. We have determined that these excess blockages have a significant clinical impact with further lines being inserted after blockage, resulting in increased risks to patients, wasted time and cost of resources. Our findings suggest that the current</p>

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	UK guidance favouring NS flushes should be reviewed.

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13 14 15 **Finding a Solution:** 16

17 18 **Heparinised saline versus normal saline in the maintenance** 19 20 21 22 **of invasive arterial lines in intensive care** 23 24 25 26 27 28

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43

44 **Key Words:** Arterial Lines; Heparin; Patient Safety
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Summary

Background

We assessed the impact of heparinised saline (HS) versus 0.9% normal saline (NS) on arterial line patency. Maintaining the patency of arterial lines is essential for obtaining accurate physiological measurements, enabling blood sampling and minimising line replacement. Use of HS is associated with risks such as thrombocytopenia, haemorrhage and mis-selection^{1,2}. Historical studies draw variable conclusions but suggest that NS is at least as effective at maintaining line patency, although recent evidence has questioned this³.

Methods

We conducted a prospective analysis of the use of HS versus NS on unselected patients in the intensive care of our hospital. Data concerning duration of 471 lines insertion and reason for removal was collected.

Results

We found a higher risk of blockage for lines flushed with NS compared with HS (RR= 2.15, 95% CI 1.392 to 3.32, $P < 0.001$). Of the 56 lines which blocked initially (19 HS and 37 NS lines), 26 were replaced with new lines. Eight heparinised lines were replaced and 18 NS lines. Five of these replaced lines subsequently blocked again, all of which were heparinised lines.

Conclusions

Our study demonstrates a significantly important reduction in arterial line longevity when flushed with NS compared to HS. We have determined that these excess blockages have a significant clinical

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Introduction

Arterial lines are routinely inserted in the critically ill patient for continuous blood pressure monitoring, frequent blood sampling and assessment of arterial oxygenation. Biochemical and physiological measurements obtained from arterial lines affect clinical decision-making and assist in evaluating patient response to clinical intervention. Maintenance of arterial line patency is essential to reduce the patient discomfort, time and financial expense incurred by blocked catheter replacement^{1,3}. Multiple factors including catheter flush solution have been shown to influence arterial line patency, with heparinised saline (HS) traditionally being used for its anticoagulant properties^{4,5}.

Current evidence regarding flush solution is conflicting, and uncertainty exists as to which solution is best. In 2008, the National Patient Safety Agency (NPSA) published a report recommending exclusive use of 0.9% normal saline (NS) as an arterial flush solution: subsequently use of HS in UK adult intensive care units has reduced to 4.6%⁶. Despite this, serious errors involving administration of incorrect arterial flush solutions continue to occur^{6,7}.

In a recent publication, catheters flushed with HS had an increased lifespan and a significantly reduced likelihood of blockage². This prompted suggestion that current debate should not only focus on patient safety, but also on the implications of widespread use of NS flushes on patient morbidity⁸. At our university teaching hospital, HS is used as a flush solution. The aim of our study was to assess the impact of HS versus NS on arterial line patency and to perform a cost analysis of their use.

Methods

The study was considered a service evaluation, therefore ethics committee approval was not required.

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3 We conducted a prospective study analysing the use of HS and NS in maintaining invasive line
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5 patency. Over a four month period in 2014, data was recorded on all unselected elective and
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7 emergency admissions to the general adult ICU of our university teaching hospital. During the first
8
9 and fourth months, data was collected on the use of HS to maintain central venous, arterial, PiCCO
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11 and VasCath line patency. After a changeover period, HS was substituted for NS for the second and
12
13 third months. Data concerning duration of line insertion and reason for line removal was collected
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15 from either our clinical information systems Innovian® or Phillips Intellispace Critical Care and
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17 Anesthesia® and details were clarified with bedside nursing staff where required.

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21 Line insertion technique and site of insertion were unstandardised and lines were inserted in a
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23 variety of settings including intensive care, operating theatres and the Emergency Department. All
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25 lines were maintained and sampled using standard hospital protocols. Both NS and HS (2 units ml⁻¹)
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27 were infused at a rate of approximately 3 mls hr⁻¹ with 300 mmHg pressure applied to infuser bags.
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31 Due to the small number of PiCCO and VasCath lines inserted and a change in the manufacturer of
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33 central lines during our study period, these lines were excluded from our analysis. A subgroup
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35 analysis was performed on occluded arterial lines, defined as lines with an unreliable arterial
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37 waveform and lines from which arterial blood samples could not be aspirated.
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40 Cost analysis was performed using the cost of all the equipment purchased in our department.
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43 The demographic (sex and age) and clinical characteristics (admission type, nature of surgery,
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45 APACHE score, ICNARC score and where the first line was placed) of the two patient groups were
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47 compared using Fisher's exact test for categorical variables and Mann Whitney U test for continuous
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49 variables. The lifespans of the lines were compared using Mann Whitney U-test to compare all lines
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51 and to compare first lines only. Cox proportional hazards regression was used to compare the
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53 survival time for lines flushed with NS compared with HS. The following analyses were undertaken to
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55 test whether differences in length of insertion persisted when restricting the reason for line removal
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57 to blockages only. The lines were further restricted to a comparison of the first lines inserted in
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3 patients to exclude the potential inflation of effect sizes due to patient-level influences on line
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5 survival.

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7 1. Failure = Replacement of any line for any reason (lifespan of line considered censored if
8 patient died)
- 9
10 2. Failure = Replacement of any line due to blockage (all other reasons considered censoring).
11 Assumed blockage = '2A - blocked (no trace)' or '2B - blocked (no blood)'.
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- 13 3. As in 2 but restricted to 1st line received - sensitivity analysis in case patient-level factors
14 affect the survival time of lines.
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20 Risk ratios were derived to compare the risk of lines blocking when flushed with NS compared with
21 HS. For reasons outlined above, we also undertook sensitivity analyses by restricting to the first lines
22 inserted in patients.
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30 Results

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33 Data from 337 patients who received 471 arterial lines were included in this study. Of these arterial
34 lines, 244 (51.8%) were flushed with HS and 227 (48.2%) were flushed with NS. The patient groups
35 were closely matched with respect to demographics (Table 1). There were multiple reasons for line
36 removal (Table 2): most commonly due to the line no longer being required (53.9%) and the line
37 becoming blocked (16.6%). We had no cases of distal limb ischaemia.
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42 The median lifespan of all lines was 2 days (1 - 4). Lines flushed with HS had a slightly longer lifespan
43 (median = 2 days, IQR = 1 - 4) compared with those flushed with NS (median = 2 days, IQR = 1 - 4) (P
44 = 0.035). Restricting to the first line inserted in each patient the median lifespan was 2.5 days (IQR =
45 1 - 4) for lines flushed with HS compared with a median of 2 days (IQR = 1 - 3) for those flushed with
46 NS (P = 0.004). The risk ratio showed a higher risk of blockage for lines flushed with NS compared
47 with HS (RR= 2.15, 95% CI 1.392 to 3.32, P <0.001), with a similar finding when restricting to only the
48 first line inserted into each patient (RR= 2.03, 95% CI 1.219 to 3.381, P=0.005).
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5 Of the 56 lines which blocked initially (19 HS and 37 NS lines), 26 were replaced with new lines: eight
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7 HS lines were replaced and 18 NS lines. Five of these replaced lines subsequently blocked again, all
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9 of which were heparinised lines. One of these replaced lines blocked for a third time.
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14 The hazard ratio for the time to failure for any reason of lines flushed with NS compared with HS was
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16 1.179 (P=0.076), indicating that lines flushed with HS last longer than those flushed with NS. The
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18 hazard ratio was higher when we restricted the reason for failure to blockages (HR = 2.471, P
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20 <0.001), and further restricting to only the first line inserted into each patient the hazard ratio was
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22 2.734 (P <0.001). The Kaplan-Meier analyses further demonstrate the line survival with relation to
23
24 flush solution (Plot 1 and Plot 2).
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27 In using NS as a flush solution, our department saved £950 in one month, thus creating a projected
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29 saving of £11,400 per annum. An average of 100 lines are inserted per month on our ITU. If all of
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31 these lines were flushed with NS, with its associated increased rate of blockage, a further £547
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33 would be incurred through catheter replacement, equating to £6,564 per annum. Balancing this
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35 against the reduced cost of NS flush solution, an overall saving of approximately £403 per month
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37 would be made which equates to £4,836 per year. This figure however, has to be weighed against
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39 the associated increased patient morbidity with NS use. In addition, for the number of lines that
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41 were replaced, there were a larger number that were not and the risk of harm as a result of this is
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43 difficult to quantify.
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46 47 48 49 **Discussion**

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52 We have demonstrated a statistically significant increase in risk of line blockage when flushing lines
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54 with NS rather than HS. Further to this, the lifespan of lines flushed with NS are significantly reduced
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56 compared to HS.
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3 High quality evidence on this area is lacking. A meta-analysis performed in 1998 demonstrating an
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5 increased longevity of lines flushed with HS⁹. This include one of which is the largest study to
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7 date – a multicentre unblinded randomised control trial from the American Association of Critical
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9 Care Nurses¹⁰. The authors analysed the 5139 subjects and concluded that heparinised lines had a
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11 significantly higher probability of remaining patent, compared to NS lines. Subsequent smaller
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13 studies have failed to demonstrate a statistically significant difference between the two flush
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15 solutions^{1,11,12,13}. These studies are heterogeneous with variable heparinised flush
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17 concentrations, sample sizes often less than 100 and few achieving adequate statistical power.
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19 A 2104 Cochrane review emphasised that NS is comparable to HS for maintaining catheter patency
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21 and re-emphasised the poor quality of existing evidence³. More recently Tully et al demonstrated an
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23 increased lifespan and a significantly reduced likelihood of blockage in lines flushed with HS².
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28 Our single centre study allowed for standardisation of equipment, procedures and data collection.
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31 Whilst there was an overall cost saving with the use of NS, the potential clinical impact with patients
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33 being inadequately monitored for periods of time the line was being replaced. Use of NS also
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35 resulted in an increased consumption of resources, including clinician's time and line replacement
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37 itself was associated with an increased morbidity to the patient. The potential misidentification of
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39 NS for a dextrose solution is additionally an ever-present risk and cases of iatrogenic
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41 neuroglycopenia are well documented locally and nationally. Inadvertent use of dextrose
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43 containing solutions leads to an artefactually raised glucose on sampling, thus prompting IV insulin
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45 administration and subsequent hypoglycaemia. This prompt the 2014 publication of an AAGBI
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47 guideline calling for stricter practical measures and changes in labelling to minimise this risk¹⁴.
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51 Based on our findings and its distinctive labelling, we argue that HS would in fact be the best and
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53 safest option despite the small risk of side effects, such as HIT, the risk of sampling contamination
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55 affecting clotting tests and its expense.
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3 Our data was predominantly collected from documentation, and therefore this may limit the
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5 accuracy of our results, however, ambiguity was clarified with nursing staff in real time. Rewiring of
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7 lines was sometimes recorded as a new line or not at all leading to some data not being captured.
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9 Recording of line duration was made in whole days due to lack of accurate recording, especially
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11 when lines were inserted outside of the ITU, for example in theatres. We did not investigate the use
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13 of concomitant anticoagulants as a confounding factor.
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17 We have added to the body of evidence on this subject. There is need for a significantly powered
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19 randomised control trial to conclude if arterial lines flushed with heparinised flushed arterial lines
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21 have statistically lower blockage rates and increased longevity compared to NS.
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24 25 26 27 **Conclusions**

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29 Our study demonstrates a significantly important reduction in arterial line longevity when flushed
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31 with NS compared to HS. We have determined that these excess blockages have a significant clinical
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33 impact with further lines being inserted after blockage, resulting in increased risks to patients,
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35 wasted time and cost of resources. Our findings suggest that the current UK guidance favouring NS
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37 flushes should be reviewed.
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44 45 **Authors Contribution**

46
47 ME (study design, patient recruitment, data collection, data analysis, writing up of the paper);

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49 LW (patient recruitment, data collection, data analysis, writing up of the paper);

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51 CP (data analysis, writing up of the paper);

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53 DFT (study design, patient recruitment, data collection, data analysis, writing up of the paper).
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John Warburton – scientific advisor

Chris Sajdler – data collection

Catherine Stace – data collection

Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest.

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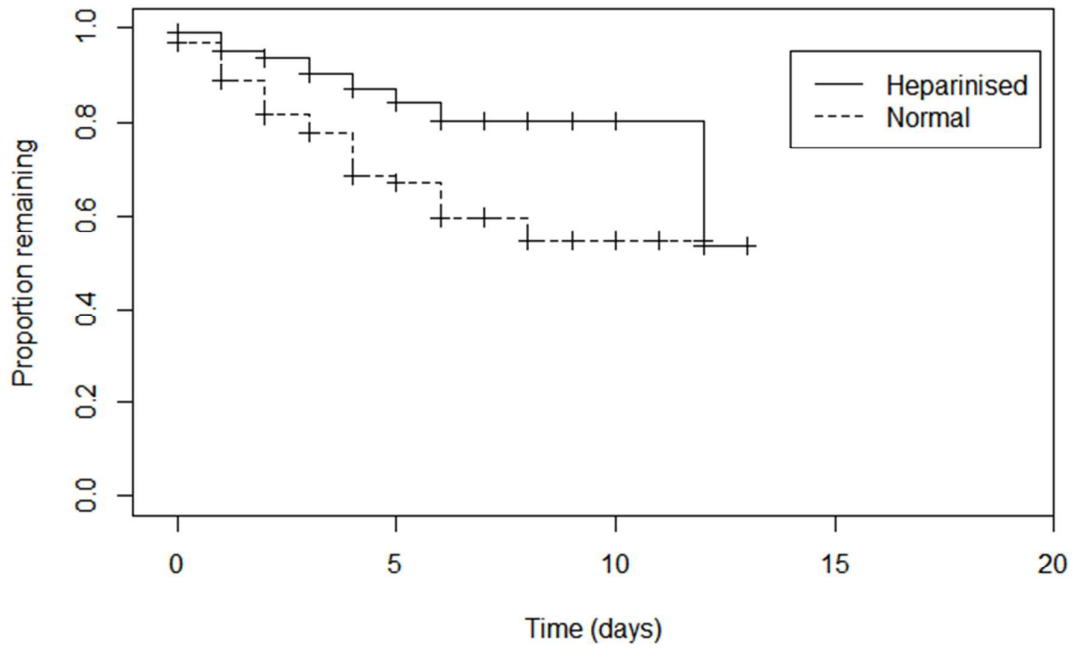
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Plot 1. Kaplan-Meier survival curve for all lines placed, failure = line blocked



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Plot 2. Kaplan-Meier survival curve for first lines placed only, failure = line blocked

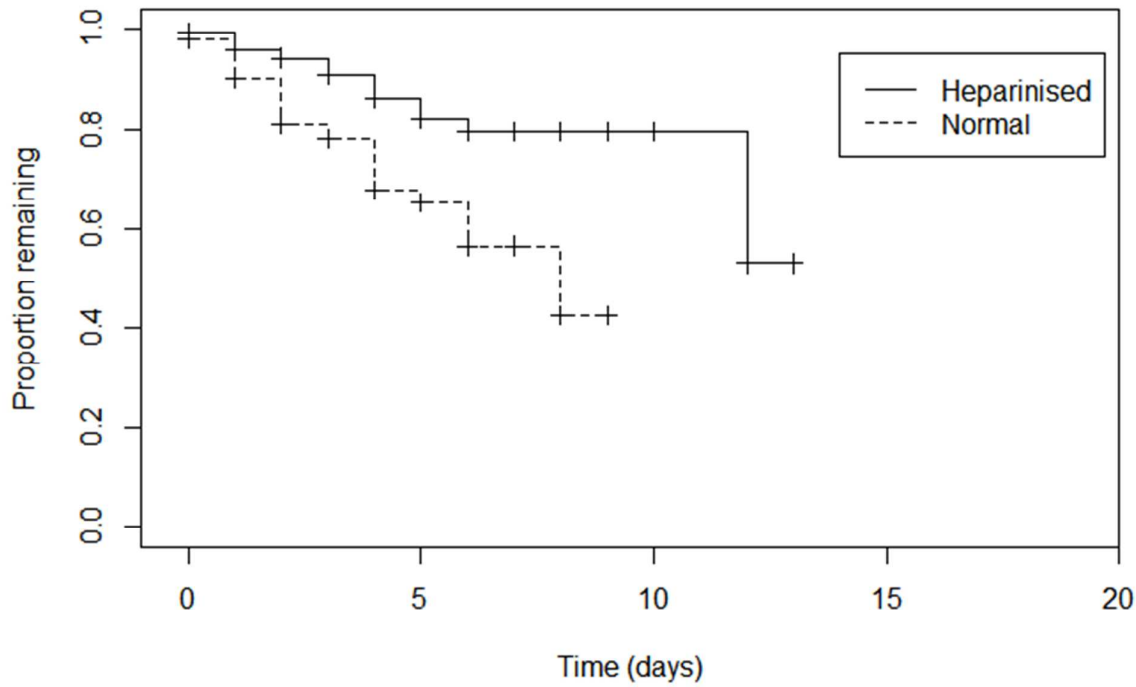


Table 1. Demographics of patients with lines flushed with Heparinised Saline versus Normal

Saline

	Heparinised Saline (172)	Normal Saline (165)	Total (337)	p-value
Age	60.7 (\pm 14.9)	61.5 (\pm 16.1)	61.1 (\pm 15.5)	0.59
Sex				0.58
Female	71 (41.3%)	63 (38.2%)	134 (39.8%)	
Male	101 (58.7%)	102 (61.8%)	203 (60.2%)	
Admission type				0.50
Unplanned	111 (64.5%)	109 (66.1%)	220 (65.3%)	
Planned	61 (35.5%)	56 (33.9%)	117 (34.7%)	
Nature of surgery				0.69
Emergency/Urgent	18 (10.5%)	12 (7.3%)	30 (8.9%)	
Scheduled/Elective	61 (36.5%)	56 (33.9%)	117 (34.7%)	
Not relevant	93 (54.1%)	97 (58.8%)	190 (56.4%)	
APACHE score	10.1 (3.8 - 34.1)	8.8 (3.4 - 34.4)	9.6 (3.8 - 34.4)	0.84
ICNARC score	11.3 (3.8 - 41.9)	10.1 (3.7 - 48.0)	10.9 (3.8 - 45.1)	0.97
Line site				0.69
Brachial	18 (10.5%)	15 (9.1%)	33 (9.8%)	
Femoral	4 (2.3%)	6 (3.6%)	10 (3.0%)	
Radial	150 (87.2%)	144 (87.3%)	294 (87.2%)	

Table 2. Reason for line removal

	Heparinised Saline (244)	Normal Saline (227)	Total (471)
Reason for removal			
1 - no longer required	144 (59.0%)	110 (48.5%)	254 (53.9%)
2A - blocked (no trace)	9 (3.7%)	23 (10.1%)	32 (6.8%)
2B - blocked (no blood)	17 (7.0%)	29 (12.8%)	46 (9.8%)
3 - infected	11 (4.5%)	5 (2.2%)	16 (3.4%)
4 - pulled/fallen out	23 (9.4%)	19 (8.4%)	42 (8.9%)
5 - leaking	12 (4.9%)	5 (2.2%)	17 (3.6%)
6 - discharged in situ	6 (2.5%)	9 (4.0%)	15 (3.2%)
7 - deceased	11 (4.5%)	25 (11.0%)	36 (7.6%)
8 - routine line change	5 (2.0%)	2 (0.9%)	7 (1.5%)
9 - unknown	6 (2.5%)	0 (0.0%)	6 (1.3%)