ISHLT JOURNAL WATCH
October 2022 | MCS + Pharmacy

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Risk factors for bleeding complications during veno-venous extracorporeal membrane oxygenation as a bridge to recovery

Kawauchi A et al. *Artif Organs.* 2022;46:1901-11.

Study Highlights

Are platelet count, APTT or mobility associated with increased risk of bleed while on VV-ECMO

Single center retrospective analysis from 2012 to 2020 at Japanese Red Cross Maebashi Hospital

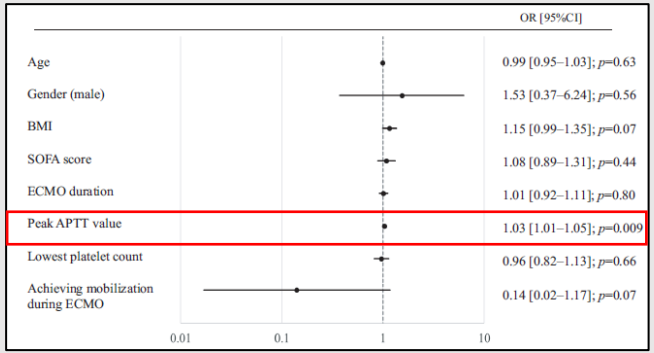
Bleeding:
- Hgb ↓ 2 g/dL in 24 hrs
- Transfusion of 4+ units of RBC
- Retroperitoneal, airway or intracranial
- Bleeding requiring surgical intervention

Thrombosis:
- Clots requiring circuit replacement
- Venous thromboembolism
- Cerebral infarction
- Bowel ischemia

Exclusion: pediatrics, VV-ECMO only for elective procedure, death within 24 hr of cannulation, admission for coronavirus infection

Central Figure

Variables	Bleeding group ($n = 31$)	Non-bleeding group ($n = 28$)	p value
Patients experienced thrombotic complication before the bleeding complication[a]	10 (32%)	10 (36%)	0.79
Patients experienced thrombotic complication during ECMO[b]	21 (68%)	10 (36%)	0.0069
Blood transfusion products use during ECMO			
Red blood cell[c] (units)	24 [13–58]	15 [8–23]	0.01
Fresh frozen plasma[d] (units)	16 [4–40]	8 [0–21]	0.03
Platelet concentrate[e] (units)	20 [8–85]	10 [0–33]	0.06
Length of ECMO (days)	21 [10–46]	8 [6–10]	<0.001
Length of ICU stay (days)	31 [16–65]	18 [11–27]	0.02
Length of hospital stay (days)	50 [33–81]	42 [23–85]	0.45
In-hospital mortality	11 (35%)	7 (25%)	0.41
28 days mortality	6 (19%)	4 (14%)	0.73
Total hospital costs[f] (US$)	80 414 [56 084–132 240]	66 460 [47 633–88 192]	0.08



Reviewer's Comments

This study was able to assess previously described risk factors for bleeding (low platelets, APTT values) and a new risk factor of mobility on ECMO. They found that peak APTT is a risk factor for bleed.

Patients with bleeding on VV-ECMO had more thrombotic events, blood products, longer ECMO and ICU length of stay, greater hospital cost.

Study Limitations

- Single center, retrospective and relatively small sample size
- Use of APTT in place of anti-Xa monitoring
- Exclusion of coronavirus infections

Conclusions

Further studies should be performed with larger cohorts to further validate risk factors for bleeding complications while receiving VV ECMO

Abbreviations: APPT activated partial thromboplastin time, VV ECMO veno-venous extracorporeal membrane oxygenation, Hgb hemoglobin, RBC red blood cells

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Conservative initial postoperative anticoagulation strategy after HeartMate 3 left ventricular assist device implantation

Damman K et al. *Neth Heart J.* 2022 April 5. doi: 10.1007/s12471-022-01671-1.

Study Highlights

Background:

- Post LVAD implantation, anticoagulation therapy is required
- Common post-operative complications include bleeding and reoperation

Methods:

- Single centre study
- November 2016 to June 2020
- Full dose LMWH bridging with vitamin K antagonist (VKA) versus VKA alone immediately post LVAD HM3 implantation

Results:

48 patients were treated with the rigorous protocol (LMWH + VKA), 25 with the conservative (VKA)

- 16/48 (LMWH +VKA) versus 1/25 (VKA) bleeding events requiring operation (p=0.002)
- No thromboembolic events in either group 1 year postoperatively

Conclusions:

Anticoagulation can be started conservatively after HM3 implantation, reducing bleeding rates without an increase in thromboembolic events.

Central Figures

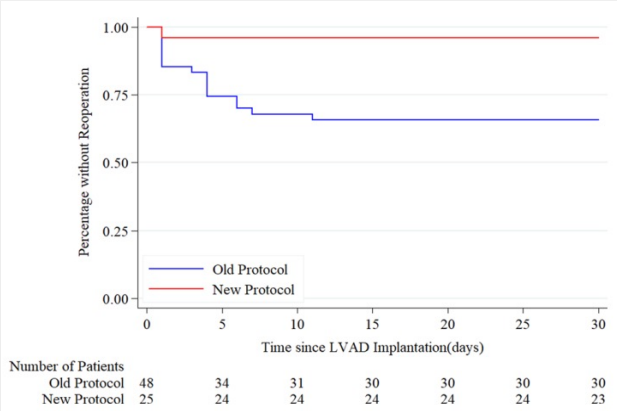

Fig. 3 Kaplan-Meier curves for time to first bleeding/tamponade event requiring reoperation after left ventricular assist device (LVAD) implantation in old and new protocol groups. P-value for long-rank test for difference between anti-coagulation protocols is 0.006

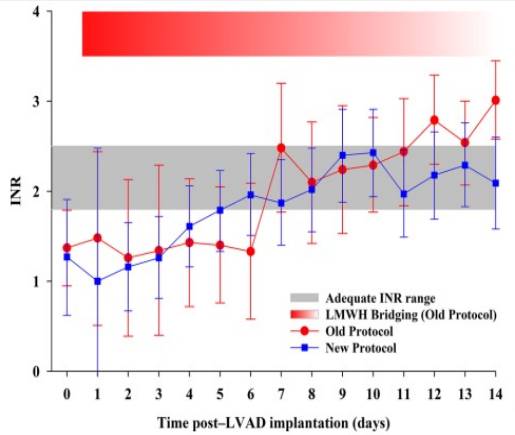

Fig.1 International normalised ratio (INR) levels after left ventricular assist device implantation in old and new protocol groups. Means and 95% confidence intervals obtained from repeated measures mixed modelling are shown. P-value for interaction type of anticoagulation protocol x times is 0.50. LMWH low molecular-weight heparin

Limitations

- Retrospective single centre open study reviewing a change in practice
- Patients on the rigorous protocol were more likely to have risk factors for bleeding
- Prophylactic dose LMWH was used in the conservative group if mobility was poor, but number of patients who received this was not reported

Reviewer's comments

- Promising results showing a significant improvement in post-HM3 implantation bleeding rates with VKA alone.
- INR control was consistent if not improved under the new protocol.
- A multi-centre study reviewing a conservative anticoagulation protocol is required to provide assurance of its safety.

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Pre-operative risk factors for driveline infection in left ventricular-assist device patients

Köhler A-K et al. *ESC Heart Failure.* 2022 April 23. doi: 10.1002/ehf2.14112.

Study Highlights

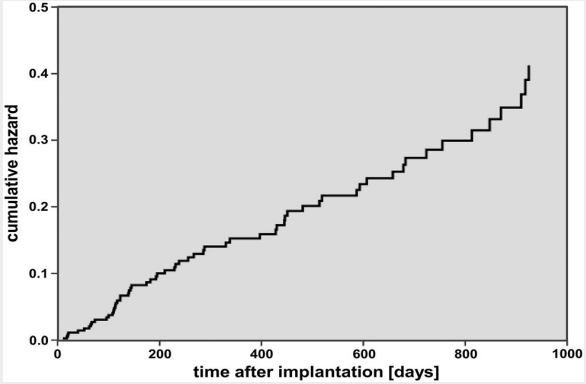
Background
Left ventricular-assist device (LVAD) driveline infections (DI) are a common adverse event after implantation. Are there any identifiable risk factors for infection?

Method
- Single centre retrospective cohort of 390 patients
- August 2009 to October 2013
- Heartmate II or Heartware
- Cohorts: infection (4 categories: “secured”/“likely”/“possible”/”unlikely”) or no infection
  - Patients with “secured” or “likely” infection (n = 61) compared vs the no infection (n = 329) cohort using a Cox proportional hazard model
- Variables tested include:
  - Age, LVAD type, creatinine, diabetes, BMI, depression, thoracic surgery following implantation

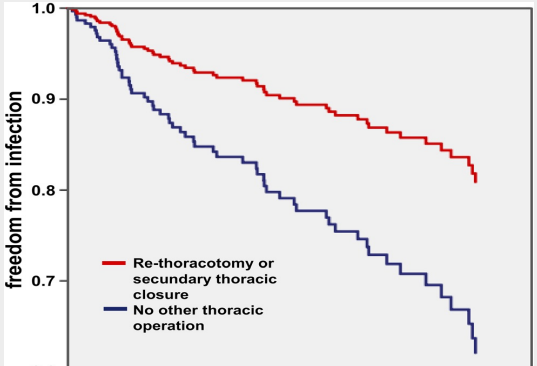
Results
- 61 (15.6%) recipients developed a DI
- Average time to DI 331 ± 273 days
- Most variables tested showed no significant effect on incidence of DI

Protective effects against DI:
- Thoracic surgery following implantation (hazard ratio [95% CI] = 0.45 [0.21–0.95]; p = 0.04)
- Creatinine level (hazard ratio [95% CI] = 0.64 [0.43-

Central Figure



Cumulative hazard for developing a LVAD DI dependent on length of time after implantation



Reviewer’s comments

- Protective effect of another thoracic operation against DI has been previously demonstrated in other studies.
- The study showed a higher pre-op creatinine level was associated with lower DI rates (in contrast to other studies).
- Risk associated with dialysis was not considered

Limitations

- Pre-op creatinine level used as a measure of renal function instead of GFR or dialysis requirements
- Difficult to retrospectively categorise DI

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Early clinical experience with nirmatrelvir/ritonavir for the treatment of COVID-19 in solid organ transplant recipients

Salerno DM et al. *Am J Transplant.* 2022;22:2083-88.

Study Highlights

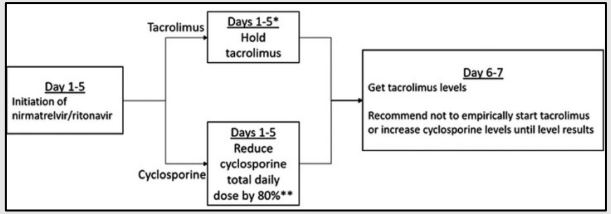
What is the efficacy of N/R for the treatment of mild COVID-19 and the impact of the DDI associated with therapy

Single center retrospective analysis of all SOT recipients receiving N/R from Dec 28, 2021 to Jan 6, 2022

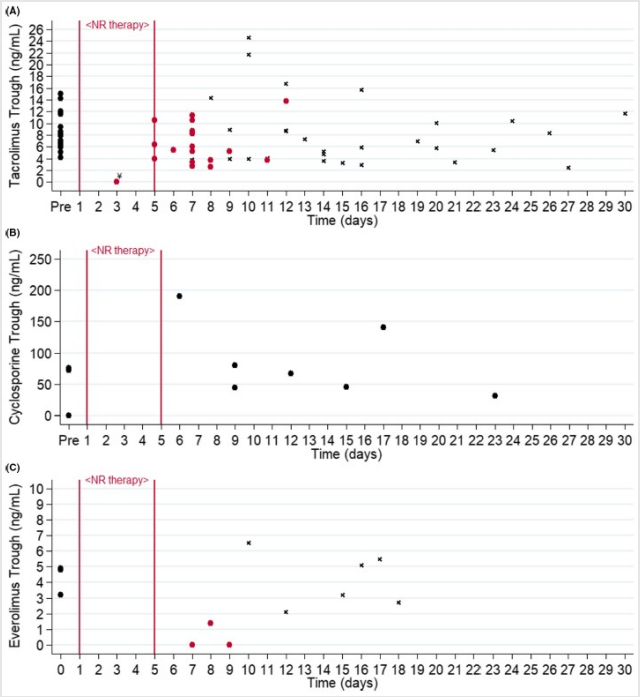
Background

- Ritonavir is a potent CYP-3A and PGP-inhibitor
- CNI and mTOR levels are impacted by these interactions

Previously Published Protocol



Central Figure



Reviewer's Comments

This study importantly shows the feasibility of N/R with CNI and mTOR therapy. Incidence of hospitalization and death was greater in this cohort compared to the general population in the EUA study.

Tac/mTOR	Hold for duration of therapy, check level before reinitiating therapy*
CSA	Reduce dose to 20% of daily dose prior to initiation of N/R therapy. Check level prior to re-increasing dose*

*For patients with high immunologic risk, consider level prior to discontinuation of N/R therapy

Abbreviations: N/R nirmatrelvir/ritonavir, SOT solid organ transplant, CNI calcineurin inhibitor, mTOR mammalian target of rapamycin inhibitor, PGP P-glycoprotein, Tac Tacrolimus, CSA cyclosporine