Perioperative Anticoagulation in Lung Transplantation and/or VV ECMO

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Lung transplantation

- Lung transplantation
  - last treatment option in
    several end-stage lung diseases
- Global transplant volume increasing
- Post-transplant survival outcome improving

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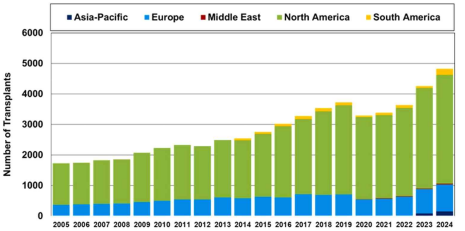
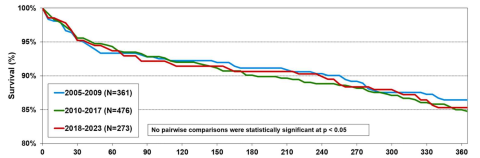
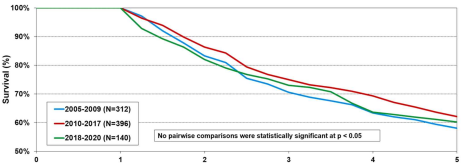




Note: The Y-axis is truncated to better highlight the differences in survival rates.

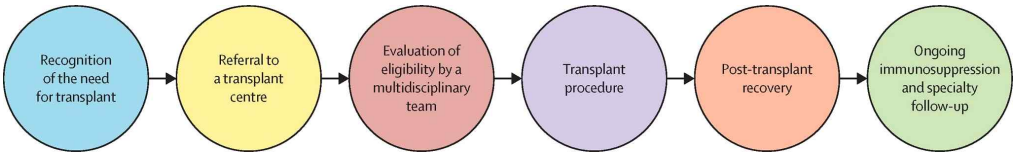


Note: The Y-axis is truncated to better highlight the differences in survival rates.

J Heart Lung Transplant. 2026

Overall process of solid organ transplantation

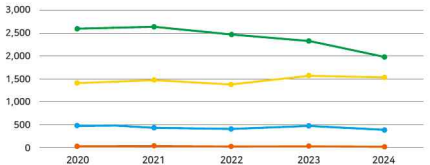
- Recognition of candidate patient
- Referral to transplant center
- Listing and waiting for organ offer
- Transplant surgery and post-transplant care



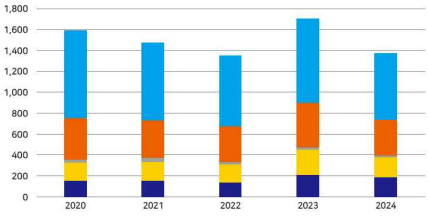
Lancet. 2025

Lung transplantation in Korea

- Annual number of deceased donor around 400
  - relatively low compared to Western countries
- Lung utilization rate around 40~50%
  - relatively high compared to Western countries



구분	2020	2021	2022	2023	2024	전년대비증감율
뇌사	478	442	405	483	397	▼17.8
사후	29	42	25	38	10	▼73.7
생존	2,585	2,645	2,468	2,339	1,980	▼15.3
조혈모	1,409	1,487	1,373	1,571	1,544	▼1.7
계	4,501	4,616	4,271	4,431	3,931	▼11.3



구분	2020	2021	2022	2023	2024	전년대비증감율
신장	848	747	677	814	644	▼20.9
간장	395	357	342	420	342	▼18.6
췌장	32	37	31	24	12	▼50
심장	173	168	167	245	194	▼20.8
폐	150	167	136	202	185	▼8.4
계	1,598	1,476	1,353	1,705	1,377	▼19.2

KONOS data

Pre-transplant waiting in Korea

- Longer waiting period due to relative shortage of deceased donor
- Transplant priority determined mainly by disease severity & urgency
- Korean lung allocation system – status system
- Transplantation in status 0 is common – bridge to lung transplant

Status	Description
Status 0	Patient is connected to a ventilator or ECMO
Status 1	One of the following: • NYHA stage IV patients with average pulmonary artery pressure >65 mmHg, NYHA stage IV patients with average right atrial pressure of >15 mmHg • NYHA stage IV patients with PaO_2 of <55 mmHg on room air • Cardiac Index <2 L/min/m^2
Status 2	One of the following: • Forced expiratory volume in 1 second <25% • PaO_2 <60 mmHg in room air • Average right atrial pressure: 10–15 mmHg • Average pulmonary artery pressure: 55–65 mmHg • Cardiac Index: 2–2.5 L/min/m^2 • Previous LT • Previous lung volume reduction surgery • Lung cancer
Status 3	Patient requiring a LT with none of the above conditions

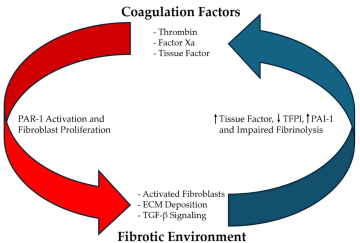
구분	2020	2021	2022	2023	2024
평균	238	215	265	292	260
A	236	226	200	260	272
B	171	266	334	317	171
O	426	237	412	383	414
AB	130	60	104	156	143

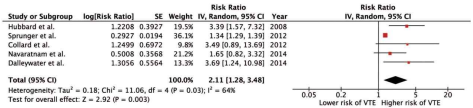
구분	2020	2021	2022	2023	2024
계	150	167	136	202	185
Status0	101	124	78	112	92
Status1	45	42	56	89	87
Status2	2	1	2	1	2
Status3	2				4

KONOS data

Issue of anticoagulation in waiting period

- Association between pulmonary fibrosis (most common indication) & thrombosis
  - molecular interaction
  - systemic inflammation
  - cardiovascular comorbidities
  - reduced mobility
  - medications such as steroid





A Placebo-Controlled Randomized Trial of Warfarin in Idiopathic Pulmonary Fibrosis

Imre Noth[1], Kevin J. Anstrom[2], Sara Bristol Calvert[2], Joao de Andrade[3], Kevin R. Flaherty[4], Craig Glazer[4], Robert J. Kaner[5], and Mitchell A. Olman[2]; for the Idiopathic Pulmonary Fibrosis Clinical Research Network (IPFnet)*

[1]University of Chicago, Chicago, Illinois; [2]Duke Clinical Research Institute, Durham, North Carolina; [3]University of Alabama, Birmingham, Alabama; [4]National Jewish Medical Center, Denver, Colorado; [5]University of Texas Southwestern, Dallas, Texas; [6]Weill Cornell Medical College, New York, New York; and [7]Cleveland Clinic, Cleveland, Ohio

Rationale: Animal and human studies support the importance of the coagulation cascade in pulmonary fibrosis.

Objectives: In a cohort of subjects with progressive idiopathic pulmonary fibrosis (IPF), we tested the hypothesis that treatment with warfarin at recognized therapeutic doses would reduce rates of mortality, hospitalization, and declines in FVC.

Methods: This was a double-blind, randomized, placebo-controlled trial of warfarin targeting an international normalized ratio of 2.0 to 3.0 in patients with IPF. Subjects were randomized in a 1:1 ratio to warfarin or matching placebo for a planned treatment period of 48 weeks. International normalized ratios were monitored using encrypted home point-of-care devices that allowed blinding of study therapy.

Measurements and Main Results: The primary outcome measure was the composite outcome of time to death, hospitalization (nonbleeding, nonelective), or a 10% or greater absolute decline in FVC. Due to a low probability of benefit and an increase in mortality observed in the subjects randomized to warfarin (14 warfarin versus 3 placebo deaths; $P = 0.005$) an independent Data and Safety Monitoring Board recommended stopping the study after 145 of the planned 256 subjects were enrolled (72 warfarin, 73 placebo). The mean follow-up was 28 weeks.

Conclusions: This study did not show a benefit for warfarin in the treatment of patients with progressive IPF. Treatment with warfarin was associated with an increased risk of mortality in an IPF population who lacked other indications for anticoagulation.

Clinical trial registered with www.clinicaltrials.gov (NCT00957242).

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Idiopathic pulmonary fibrosis (IPF) is a relentlessly progressive interstitial lung disease with a median survival of 2 to 5 years from onset of symptoms. Despite multiple recent clinical trials, no definitive therapy is known to alter survival.

What This Study Adds to the Field

This study investigated the safety and efficacy of warfarin in IPF using a double-blind, placebo-controlled design. Treatment with warfarin was associated with no clinical benefit in patients with IPF.

Cells. 2024
Sarcoidosis Vasc Diffuse Lung Dis. 2018
Am J Respir Crit Care Med. 2012

Korean VTE epidemiology data

- Increased risk of VTE in pulmonary fibrosis compared to general population

J Korean Med Sci. 2022 May 02;37(17):e130. English.
Published online Apr 25, 2022.
https://doi.org/10.3346/jkms.2022.37.e130

Original Article

Incidence of Venous Thromboembolism: The 3rd Korean Nationwide Study

Hun-Gyu Hwang,[1] Ju Hyun Lee,[2] Sang-A Kim,[2] Yong-Ki Kim,[3] Ho-Young Yhim,[4] Junshik Hong,[5]
view all

Author information | Author notes | Copyright and License | Author Summary in Korean | Audio-Visual File

Abstract

Background

The incidence of venous thromboembolism (VTE) has gradually increased in the Korean population. This study aimed to evaluate the annual age- and sex-adjusted incidence rates (ASR) of VTE and anticoagulation trends between 2014 and 2018.

Methods

Using the Korean Health Insurance Review and Assessment Service database, we retrospectively identified VTE patients between 2014 and 2018 using both diagnostic and medication anticoagulant codes assigned within 6 months of the initial index event. Anticoagulant patterns were classified as follows: direct oral anticoagulants (DOAC), parenteral anticoagulants, warfarin, and mixed anticoagulation regimens.

Results

We identified 95,205 patients with VTE (female, 56.8%). The ASR for VTE per 100,000 person-years increased from 32.8 in 2014 to 53.7 cases in 2018 (relative risk of 1.63; 95% confidence interval, 1.6–1.67). The VTE incidence rates were 25 times higher in the ≥ 80 group than in the 30s group. VTE occurred 1.29 times more often in women than in men. The proportion of DOAC prescriptions increased from 40.5% to 72.8%, whereas warfarin prescriptions decreased from 27% to 5.6% in 2014 and 2018.

Conclusion

In Korea, the ASRs of VTE continued to increase since 2014, but the rate of increase slowed in 2018. The VTE occurred more often in the elderly and in women. Five years after the introduction of DOACs in 2013, they accounted for 73% of all anticoagulants used to treat VTE.

Venous thromboembolism in patients with idiopathic pulmonary fibrosis, based on nationwide claim data

Jang Ho Lee, Hoon Hee Lee, ..., and Ho Cheol Kim
View all authors and affiliations

All Articles | https://doi.org/10.1177/17534666231155772

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Abstract

Background:

Idiopathic pulmonary fibrosis (IPF) is a known risk factor for venous thromboembolism (VTE). However, it is currently unknown which factors are associated with an increase of VTE in patients with IPF.

Objectives:

We estimated the incidence of VTE in patients with IPF and identified clinical characteristics related to VTE in patients with IPF.

Design and methods:

De-identified nationwide health claim data from 2011 to 2019 was collected from the Korean Health Insurance Review and Assessment database. Patients with IPF were selected if they had made at least one claim per year under the J84.1 [*International Classification of Diseases and Related Health Problems*, 10th Revision (ICD-10)] and V236 codes of rare intractable diseases. We defined the presence of VTE as at least one claim of pulmonary embolism and deep vein thrombosis ICD-10 codes.

Results:

The incidence rate per 1000 person-years of VTE was 7.08 (6.44–7.77). Peak incidence rates were noted in the 50–59 years old male and 70–79 years old female groups. Ischemic heart disease, ischemic stroke, and malignancy were associated with VTE in patients with IPF, with an adjusted hazard ratio (aHR) of 1.25 (1.01–1.55), 1.36 (1.04–1.79), and 1.53 (1.17–2.01). The risk for VTE was increased in patients diagnosed with malignancy after IPF diagnosis (aHR = 3.18, 2.47–4.11), especially lung cancer [hazard ratio (HR) = 3.78, 2.90–4.96]. Accompanied VTE was related to more utilization of medical resources.

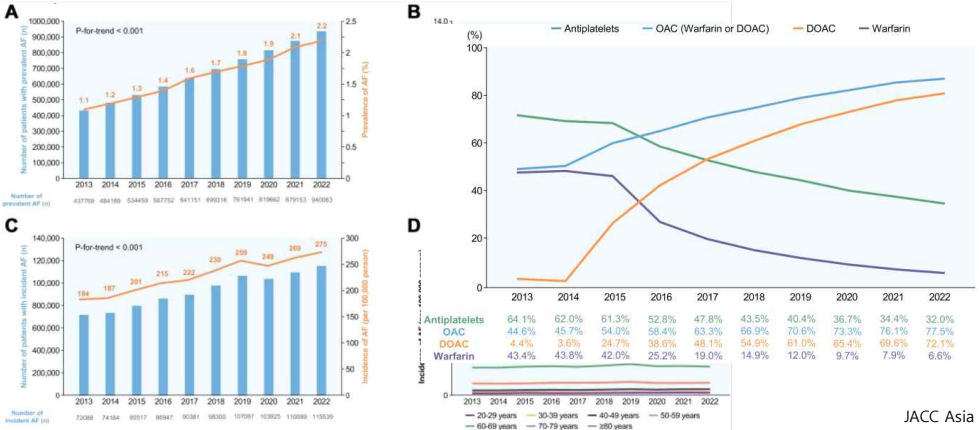
Conclusion:

Ischemic heart disease, ischemic stroke, and malignancy, especially lung cancer, were related to higher HR for VTE in IPF.

Ther Adv Respir Dis. 2023
J Korean Med Sci. 2022

Atrial fibrillation epidemiology in Korea

- Increasing prevalence & incidence of atrial fibrillation
- Candidate for lung transplant may have atrial fibrillation



JACC Asia 2025

Issue of anticoagulation in perioperative period

- Nature of lung transplant surgery
  - emergency rather than elective surgery
  - but can be anticipated to some extent

- Bridge to lung transplant – status 0
  - mechanical ventilation or ECMO at preoperative period
  - anticoagulation often needed (especially if ECMO is used)

- ECMO may be needed at postoperative period as well

Table 2. Anticoagulant Dosing based on ISTH[2]

Anticoagulant	Dose	Maintain
UFH	Bolus 50 – 100IU/kg	Continual infusion to achieve anticoagulation targets
Bivalirudin	0.02 – 0.05 μg/kg/min	Continual infusion to achieve anticoagulation targets
Argatroban	0.2 – 0.5 μg/kg/min	Continual infusion to achieve anticoagulation targets

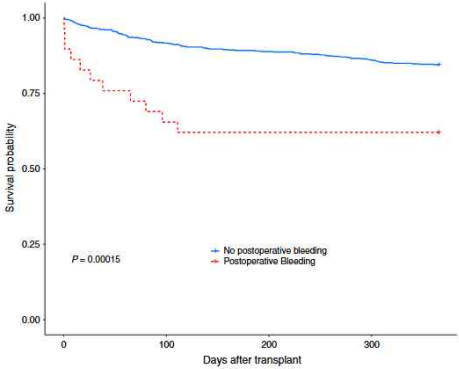
Table 3. Summary of aPTT Ranges for Practical Use[16, 19, 20, 21, 22, 23, 24, 26, 28, 37]

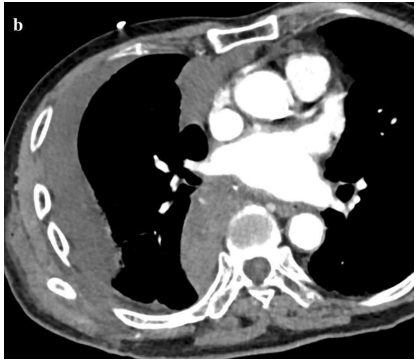
Anticoagulant	Target aPTT (Seconds)	Comments
UFH	40–80	Median ~60; most common target in ECMO.
Argatroban	50–70	Adjusted for liver function; monitoring variability possible.
Bivalirudin	50–75	Preferred for stable dosing; adjust for renal function.

JHLT Open. 2025
Intensive Care Med. 2022

Bleeding complication after lung transplant

- Perioperative bleeding complication is not uncommon
  - significant impact on morbidity & mortality



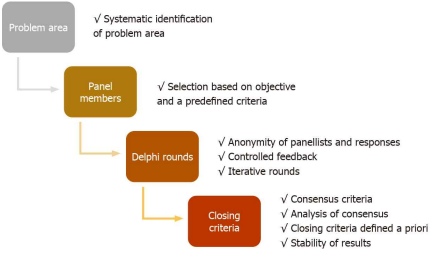


Transpl Int. 2019

Anticoagulation in this special population

- Unresolved question
  - no standardized guideline
  - lack of well-designed studies
  - critically ill patients
  - various strategies by different centers

- Development of a Korean consensus guideline
  - systematic review & meta-analysis not feasible
  - Delphi methodology ongoing



Key Questions

- Q1. 페이식 대기자 등록 시, 만약 환자가 반감기가 긴 DOAC이나 신기능에 크게 영향을 받는 약제를 복용 중이라면, 향후 응급 수술 시 빠른 배설을 대비하여 반감기가 상대적으로 짧은 약제로 변경하는 것을 권고하십니까?

- Q2. 페이식 대기 순위가 응급도 1에 도달했을 때, DOAC을 중단하고 반감기가 짧고 조절이 용이한 LMWH이나 UFH으로 전환을 미리 해두는 것을 권고하십니까?

Key Questions

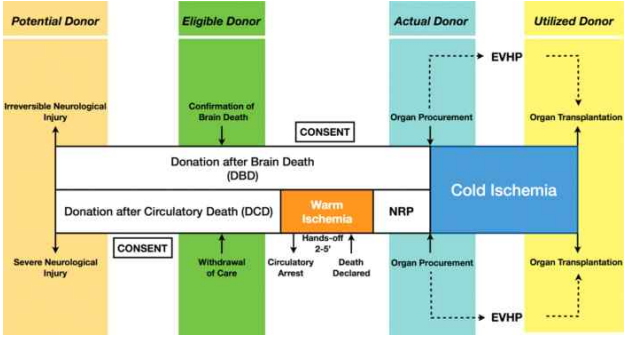
- Q3. 장기 배정 연락을 받은 즉시, 폐이식 수술 전까지 약제를 중단하는 것을 권고하십니까?

- Q4. 약제 중단을 권고 한다면, DOAC 잔류 효과를 고려하여 약제별, 신기능 별 추천된 안전중단시간을 고려하여 중단하는 것을 권고하십니까?

DOAC	Rivaroxaban	Edoxaban	Apixaban	Dabigatran
	Xarelto ®	Lixiana ®	Eliquis ®	Pradaxa ®
Target	FXa	FXa	FXa	FIIa
t ½	7–13 h	10–14 h	8–15 h	12–17 h
Cmax	2–4 h	2–4 h	2–4 h	1–2 h
Renal clearance	33% active 33% inactive	50%	25%	80%
Bioavailability	80%	62%	50%	6%
Dosing scheme	OD	OD	BID	BID
Interaction	CYP3A4, CYP2J2, P-gp	P-gp	CYP3A4 P-gp	P-gp
Interference with food	Increases AUC to 39%	None	None	Prolongs Cmax to 2 h
Antidote	Andexanet alfa	Andexanet alfa	Andexanet alfa	Idarucizumab
Allowed in pregnancy	No	No	No	No
Induces HIT II	No	No	No	No

Key Questions

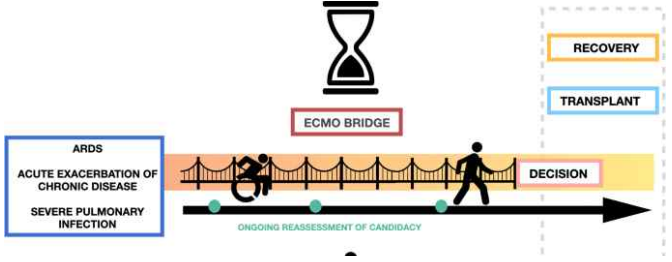
- Q5. 환자의 DOAC 잔류 농도를 감소시켜 수술 중 출혈 위험을 낮추기 위해, 적정 기증자 폐 허혈 시간 (Cold Ischemia Time) 이 허용하는 최대 한도 내에서 수술 시작 (Skin incision) 시간을 의도적으로 지연시키는 전략에 동의하십니까?



Key Questions

- Q6. 폐이식 대기 중 DOAC을 복용하고 있는 환자에서 bridging VV-ECMO 또는 VA-ECMO를 시작하는 경우 항응고 전략은 어떻게 권고하십니까?

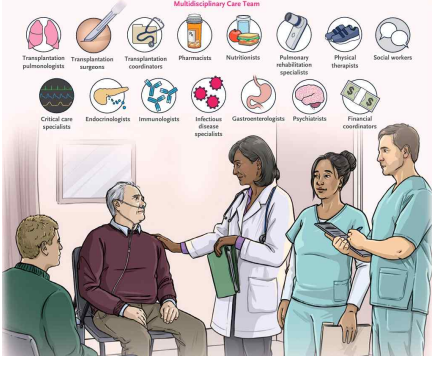
- Q7. Bridging VV-ECMO 또는 VA-ECMO로 항응고 치료를 받고 있는 폐이식 대상자에서 폐이식 직전 ECMO 항응고 전략은 어떻게 권고하십니까?

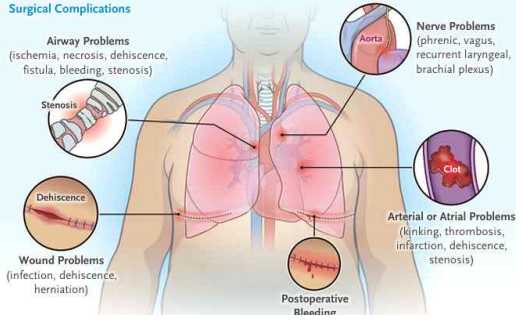


Key Questions

- Q8. 폐이식 후 ECMO를 유지 중인 환자에서 항응고 치료는 언제, 어떻게 재개하길 권고하십니까?

- Q9. 폐이식 후 ECMO를 이탈한 환자에서 DOAC은 언제, 어떻게 재개해야 한다고 생각하십니까?





Thank you for your attention