

SUPPLEMENTARY MATERIAL

For the manuscript: *Iron deficiency in patients with left ventricular assist devices*

Supplementary Table 1 – Search terms

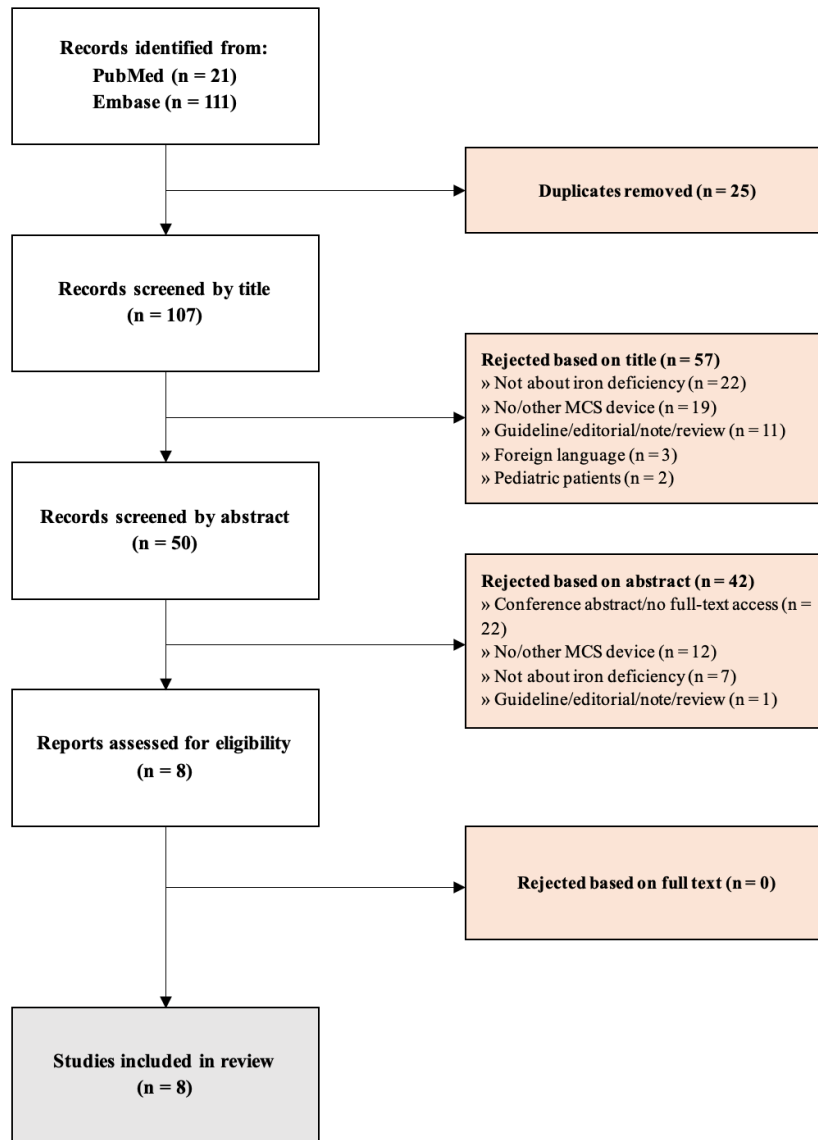
Search criteria used in the PubMed database on September 26, 2023

			Final search term
Key concept	LVAD	Iron deficiency	(LVAD* OR "ventricular assist device*" OR heartmate OR heartware OR "long-term mechanical circulatory support" OR "ventricular assist system*" OR "Heart-Assist Devices" [Mesh]) AND ("anemia, iron deficiency" [Mesh] OR iron-deficiency OR iron-deficient OR "iron repletion" OR "iron depletion" OR "iron depleted" OR "intravenous iron" OR "iron homeostasis" OR "iron metabolism" OR "iron replacement" OR "iron supplement*" OR "iron therapy" OR "iron therapies" OR "iron deficiency" OR "iron deficient" OR "iron replacement" OR "iron supplement*" OR "iron therapy" OR "iron therapies" OR "iron deficiency" OR "iron deficient" OR "iron deficient")
Free text terms	LVAD Ventricular assist device HeartMate HeartWare Long-term mechanical circulatory support Ventricular assist system	Iron-deficiency Iron-deficient Iron repletion Iron depletion Iron depleted Intravenous iron Iron homeostasis Iron metabolism Iron replacement Iron supplement Iron therapy Iron therapies Iron deficiency Iron deficient Ferric Ferrous	
Subject terms	"Heart-Assist Devices"[Mesh]	"Anemia, iron deficiency" [Mesh]	
Search results, n	21,953	134,645	21

Search criteria adapted for the Embase database resulted in 111 entries on September 26, 2023.

(lvad* or "ventricular assist device*" or heartmate or heartware or "long-term mechanical circulatory support" or "ventricular assist system*" or exp left ventricular assist device/) and (exp iron deficiency/ or exp iron deficiency anemia/ or iron-deficiency or iron-deficient or "iron repletion" or "iron depletion" or "iron depleted" or "intravenous iron" or "iron homeostasis" or "iron metabolism" or "iron replacement" or "iron supplement*" or "iron therapy" or "iron therapies" or "iron deficiency" or "iron deficient")

Supplementary Figure 1 – Flow-chart of literature search



Supplementary Table 2 – Detailed summary of included studies

		Amione-Guerra (2017) ¹⁸		Bode (2019) ⁴⁷		Bakosova (2022) ²¹	Peters (2022) ⁴⁸		Veenis (2022) ¹⁹	Vesper (2024) ²²		Bernier (2023) ²⁰	Ton (2023) ²³
Study characteristics	Study design	Cross-sectional ¹		Prospective, observational		Retrospective	Retrospective		Retrospective	Retrospective		Retrospective	Retrospective
	n ²	58		31		7	205		84	33		12	87
	Patient population	Outpatients with LVAD ≥6 months		Patients with LVAD		Patients enlisted for HTx (LVAD subgroup)	Patients with LVAD		Patients with LVAD or HTx	Patients with HM3		Patients with LVAD	Patients with LVAD
	Major inclusion criteria	Anemia (Hb <12 g/dL)		ID (FAIR-HF def.)		Consecutive patients meeting criteria for HTx-enlisting	ID (FAIR-HF def.)		≥18 years old ≥3 months follow-up	ID (Fair-HF def.)		Treated with iron ≤30 days post-implant	Plasma samples at ≥3 points (2 weeks before, 1, 3, and 6 months after LVAD implant)
	Major exclusion criteria	GI bleed/transfusion ≤3 months Conditions influencing the nature of anemia ³		Transfusions ≤3 months Signs of PT (LDH >3x normal) Active bleeding/infection		Disorders that significantly limit prognosis or serious extracardiac disease. ⁴	-		Death/HTx ≤90 days post-implant	IV iron outside of index submission Dialysis requirement at index discharge Transfusions ≤6 months		Blood transfusions ≤90 days after IV iron	-
	Follow-up	-		IV: median 42 days Oral: median 237 days		-	3 months		≤24 months (median 649 days)	≤6 months of discharge (median 83 days)		≤90 days of last dose of iron (median 46 days)	6 months
	Comparator	ID vs. non-ID anemia		IV vs. oral iron ⁵		LVAD vs. non-LVAD	IV iron vs. no IV iron		LVAD vs. HTx	IV iron vs. no IV iron		LVAD vs. non-LVAD	-
	Iron preparation(s)	-		IV ferric gluconate IV ferumoxytol Oral ferrous sulfate ⁶		-	IV iron sucrose ⁷		Not reported	IV ferric gluconate		Not reported	Not reported
Focus	Aetiology of anemia		Efficacy of IV/oral iron in correcting ID		Prevalence of ID	Safety and efficacy of IV iron		Prevalence of ID and iron supplementation in advanced HF patients	Efficacy of IV iron during index submission		Efficacy of IV iron on iron/anemia indices + compare response with control	Persisting hepcidin dysregulation	
Primary endpoints	-		Rate of resolution of ID		-	Hb at 12 weeks		-	Change in MLWHFQ and 6MWD from baseline to follow-up		Change in Hb and MCV from baseline to follow-up	-	
		Amione-Guerra (2017)		Bode (2019)		Bakosova (2022)	Peters (2022)		Veenis (2022)	Vesper (2024)		Bernier (2023)	Ton (2023)
Patient characteristics (at baseline)	Subgroup	Non-ID		ID			+iron sup.			+IV iron			
	n (%)	21 (36%)	37 (64%)	10 (32%)	21 (68%)	7 (100%)	67 (33%)	138 (67%)	84 (100%)	20 (61%)	13 (39%)	12 (100%)	87 (100%)
	Age (years)	62 ± 11	56 ± 12	56.0	56.8	54.3 ± 5.6	62 (54–69)	59 (50–68)	57.8 (52.4–62.2)	61 (56–69)	60 (47–71)	66 (45–72)	62 (62–69)
	Male sex	71%	78%	70%	91%	100%	84%	86%	79%	85%	92%	83%	82%
	Ischemic HF aetiology	52%	62%	-	-	-	40%	41%	46%	50%	46%	-	-
	LVAD												

Device	HMII		HMII	HMII HM3	-	HMII, HM3, HVAD		HMII, HM3	HM3		HM3 (58%)	HMII, HM3, HVAD
DT as indication	71%	59%	-	-	0%	72%	68%	23%	20%	85%	50%	-
Duration (months)	22 ± 16	23 ± 18	31.2	20.4	-	18.9 (7.6–29.7)	12.4 (6.7–21.5)	2.3 (0.6–6.2)	0	0	-	0
Lab results												
Hb (mmol/L)	6.8 ± 0.7	6.2 ± 0.9	6.3	7	6.6 ± 0.6	5.7 (5.3–6.6)	6.8 (6–7.9)	-	6.6 (5.5–8.2)	6 (5.7–7.8)	5.3 (5–5.6)	6.5 (5.6–7.2)
Ferritin (µg/L)	302 ± 160	74 ± 59	41.3	66.7	268 (106–368)	46 (30–117)	71 (45–104)	-	164.5 (57.7–236)	132 (73.8–204)	25 (19–52)	188 (111–417) [n=76]
TSAT (%)	27 ± 6	13 ± 6	12.7	13.9	14 ± 4	-	-	-	9.5 (8–14.5)	13.5 (8.8–17.3)	6 (5–8)	15 (11–21)
S-iron (µmol/L)	12 ± 3.6	8 ± 3.6	-	-	7.8 (5.6–9.8)	-	-	-	-	-	-	-
MCV (fL)	93 ± 8	86 ± 9	-	-	-	79 (73–86)	85 (81–90)	-	-	-	73 (70–85)	-
Creatinine (µmol/L)	-	-	111	99	89 (68–105)	115 (88–159)	106 (88–133)	151 (116–189)	97 (80–124)	133 (99–150)	-	106 (88–141)

1 = Amione-Guerra et al. also conducted a retrospective analysis but did not address ID in that part. Therefore, only the cross-sectional arm was included in this review.

2 = Number of patients with an LVAD (may only be a subgroup/arm)

3 = Myelodysplastic syndrome, Chemotherapy, hemochromatosis

4 = Infections, malignancies, peptic ulcer disease, severe kidney, liver or lung dysfunction, etc.

5 = Selection to IV vs. oral based on patient factors (i.e., cost, logistics)

6 = IV inpatients: Ferric Gluconate, 250 mg every 12 hours until corrected (per Ganzoni's formula), IV outpatients: Ferumoxytol 1020 mg over 30 minutes, PO: ferrous sulfate 325 mg (frequency determined by physician)

7 = IV Iron sucrose, 200 mg x5 or 300 mg x3 (inpatients dosed daily, outpatients dosed weekly)

Missing data is represented with "-". The presented data is either mean (± SD) or median (IQR)

DT = Destination therapy; GI = Gastrointestinal; HF = Heart failure; Hb = Hemoglobin; HMII = HeartMate II; HM3 = HeartMate 3; HTx = Heart transplantation; HVAD = HeartWare; ID = Iron deficiency; IV = Intravenous; LDH = Lactate dehydrogenase; LVAD = Left ventricular assist device; MCV = Mean corpuscular volume; PT = Pump thrombosis; S-iron = Serum iron; TSAT = Transferrin saturation