

Liver Perfusion Protocol for Supercooling Preservation

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BACKGROUND

Nearly 10,000 people in the United States are waiting for a life-saving liver transplant. Machine perfusion and supercooling potentially allow for pre-transplant donor graft optimization, longer term storage, and increased transportation distances of donor organs.

METHODS

Performed literature review on how to transition between different perfusion temperatures and integrated existing data into proposed perfusion protocol.

RESULTS

- Developed a perfusion protocol that outlined critical steps to preserve a donor liver graft transitioning between normothermia and supercooled states.
- Compiled literature review findings into a manuscript for publication that analyzed the pros and cons of current preservation and perfusion strategies under clinical investigation and use.

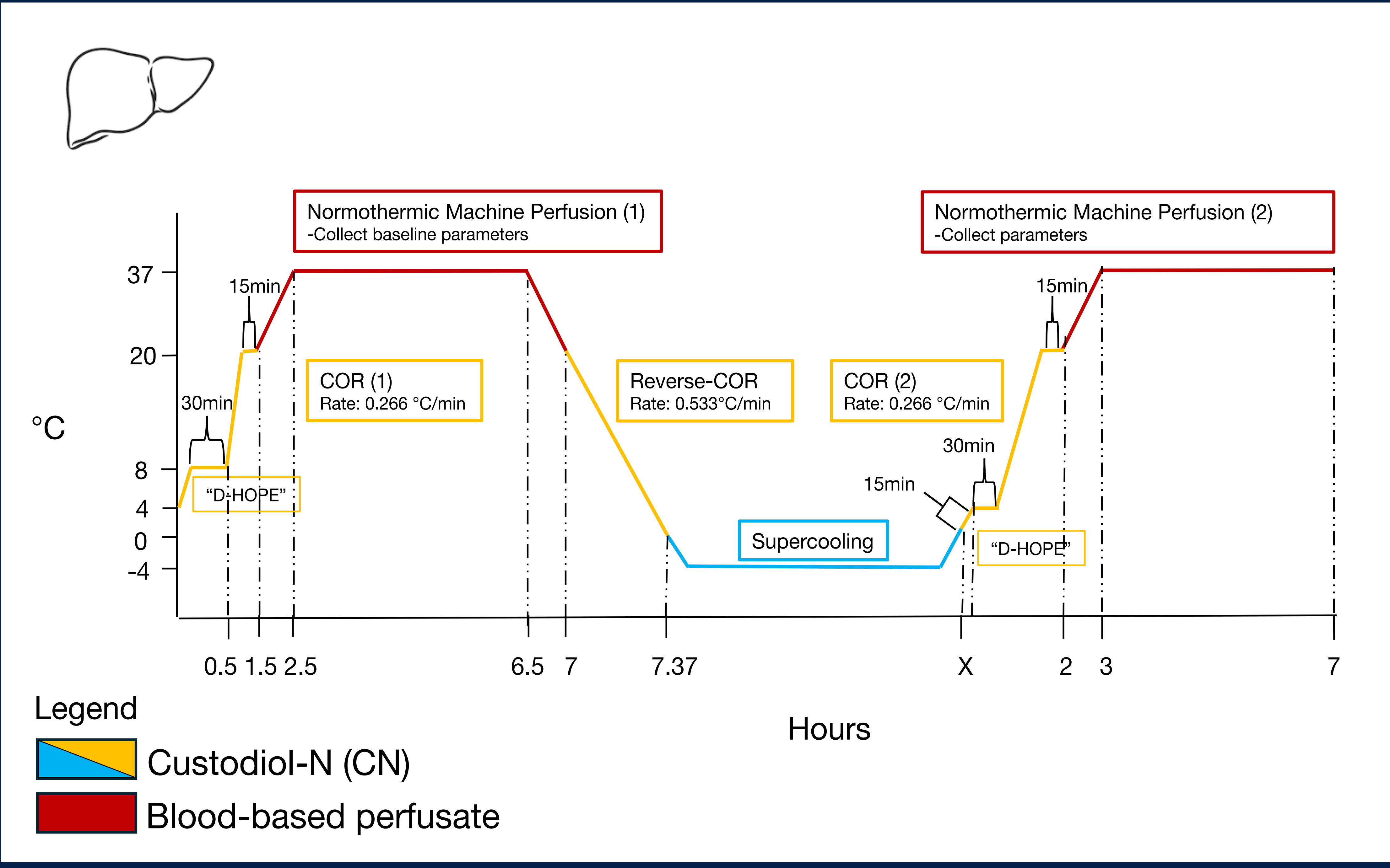
DISCUSSION

Clinical trials have shown that machine perfusion can help optimize organs that would otherwise be discarded. Supercooling may extend the preservation time of organs to days, weeks, or months. Combining these two technologies has the potential to significantly expand the donor pool and help alleviate the donor organ shortage.

ACKNOWLEDGEMENTS

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Proposed protocol to transition donor liver grafts between normothermia and supercooling



How are organs stored before transplant?

- Static cold storage (SCS) is widely used to preserve donor livers before transplant.
- Less healthy organs are more likely to experience complications after transplant and are often discarded for this reason.

Machine Perfusion

- Machine perfusion is a technique for preserving organs by actively perfusing them with perfusate.
- Several approaches have been developed to expand the donor organ pool and improve donor organ function.
- Studies suggest machine perfusion can also increase graft quality in marginal organs.

Supercooling

- Supercooling aims to reduce storage temperature below zero without ice crystal formation to depress cellular metabolism.
- The possibility of preservation times is far greater than what can be attained with machine perfusion or SCS.

Modality	C°	Media	Pros	Cons
SCS	0-4	UW, CN	- Low cost - Simple logistics - Excellent post-operative outcomes with healthy livers	- Extended hypoxia and higher chance of IRI - Particularly damaging to ECD organs 12-hour time limit
HMP	2-10	UW, CN, HBOC	- Promotes ATP recovery, clinical outcomes superior to SCS - Protects endothelial cells by upregulating nitric oxide synthase	- Cannot evaluate or condition organ - Prolonged perfusion results in endothelial damage
SNMP	20-25	CN, HBOC	- Can evaluate viability - Promotes ATP recovery, clinical outcomes superior to SCS - Less complicated metabolism demands to NMP	- Cannot condition organ - Increased oxidative stress by depleting glutathione reserves
NMP	37	HBOC, blood-based	- Potential to optimize organs via additives - Can evaluate liver function	- Requires oxygen carrier - Complex metabolism support - Expensive

SCS, static cold storage; HMP, hypothermic machine perfusion; SNMP, subnormothermic machine perfusion; NMP, normothermic machine perfusion; IRI, ischemia reperfusion injury; ECD, extended criteria donor; UW, University of Wisconsin; CN, Custodiol-N; HBOC, hemoglobin-based oxygen-carrying solution