

THE ACUTE CARE ATLAS

HALT Heart After Liver Transplantation

How the Liver Can Protect the Heart From Donor Specific Antibodies



The liver meets the antibodies first so the heart does not have to.

IN DEPTH ADVANCED TRANSPLANT PEARL

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How to Use This Guide

This guide explains why selected highly sensitized patients undergoing combined heart and liver transplantation may receive the liver before the heart. It connects the HLA antibody science to the operative sequence, postoperative surveillance, and bedside warning signs that matter to acute care clinicians.

Main conclusion:

HALT uses the donor liver as an in vivo desensitization organ. After liver reperfusion, circulating donor-specific antibodies may fall rapidly, allowing the donor heart to enter a less antibody-reactive circulation. HALT reduces risk; it does not eliminate rejection or the need for close surveillance.

What Is HALT

HALT stands for Heart-After-Liver Transplantation. It is a specialized combined heart and liver transplantation strategy considered for selected recipients who require both organs and have clinically significant preformed donor-specific HLA antibodies against the selected donor. [1]

In a conventional combined transplant, the heart may be implanted before the liver. HALT intentionally reverses that order:

1. The donor liver is implanted and reperfused first.
2. The recipient's circulation passes through the donor liver.
3. DSA and crossmatch activity may be reassessed.
4. The donor heart is implanted after antibody activity has fallen.

The sequence serves an immunologic purpose. It allows the donor liver to encounter the recipient's preformed antibody burden before the more antibody-sensitive heart is implanted.

Essential Terms

Term	Clinical meaning
HLA	Human leukocyte antigens. Cell-surface proteins that help the immune system distinguish self from non-self.
Allosensitization	Development of antibodies after exposure to non-self HLA through pregnancy, transfusion, transplantation, or other major blood-product exposure.
cPRA	Estimated percentage of potential donors against whom a recipient has unacceptable HLA antibodies.
DSA	An antibody that recognizes an HLA antigen expressed by the selected donor.
Crossmatch	A laboratory or virtual assessment of whether recipient antibodies are expected to react with donor cells.

Why Preformed Antibodies Matter

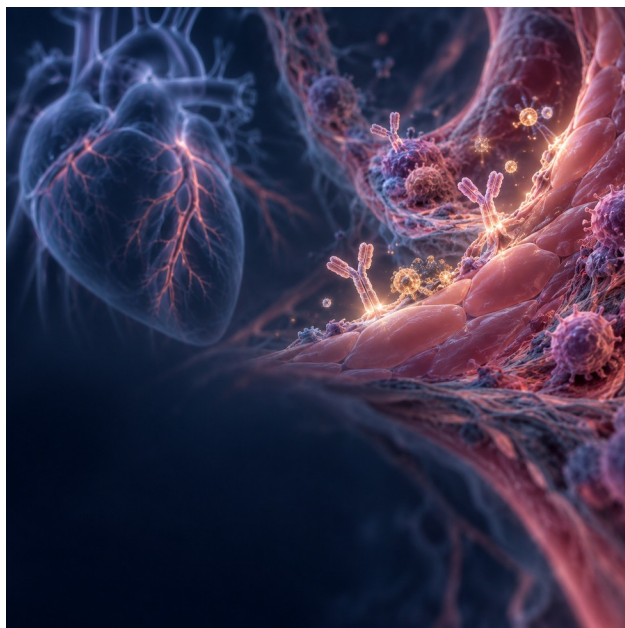
A recipient may develop anti-HLA antibodies after pregnancy, blood transfusion, previous transplantation, ventricular assist device implantation, or prior cardiac operations with substantial blood-product exposure. These exposures can prime immune memory long before a new donor is identified.

- A high cPRA indicates broad sensitization and narrows the pool of compatible donors.
- A DSA result is donor specific. It indicates that an existing antibody recognizes an HLA target on the selected donor.
- A virtual or physical crossmatch helps define the likelihood and strength of donor-directed reactivity.
- Antibody strength, class, complement-binding capacity, historic patterns, and center-specific thresholds all influence risk assessment.

What Happens in a DSA Rich Circulation

The donor heart expresses HLA on its coronary microvascular endothelium. Preformed DSA can bind those targets soon after reperfusion and initiate complement activation and inflammatory cell recruitment. Endothelial swelling, capillary leak, platelet activation, and coagulation can impair microvascular perfusion.

DSA binding › complement activation › endothelial inflammation › microvascular injury › impaired myocardial perfusion



C4d deposition may provide tissue evidence that antibodies activated the classical complement pathway, but C4d is neither perfectly sensitive nor sufficient by itself to diagnose cardiac antibody-mediated rejection. Current interpretation integrates histology, immunopathology, DSA, graft function, and clinical findings. [2,3]

How Antibody Injury Can Affect the Heart

Diffuse coronary microvascular injury may produce major myocardial dysfunction even when the epicardial coronary arteries remain patent. The clinical presentation depends on antibody burden, complement activity, the timing of injury, and the recipient's physiologic reserve.

Potential manifestations

- Myocardial edema and capillary leak
- Microvascular inflammation and intravascular macrophage accumulation
- Platelet aggregation and microvascular thrombosis
- Impaired myocardial perfusion and myocyte injury
- Acute antibody-mediated rejection or hyperacute rejection
- Biventricular dysfunction, cardiogenic shock, or early graft loss
- Later contribution to cardiac allograft vasculopathy

Important distinction:

Antibody-mediated injury can cause severe early graft dysfunction that may resemble primary graft dysfunction. When an identifiable cause such as hyperacute rejection or AMR explains the dysfunction, the team should avoid treating the label “primary” as the final diagnosis.

Why the Heart Is Vulnerable

The heart depends on continuous coronary microvascular perfusion. Widespread endothelial activation can compromise oxygen delivery across the myocardium, increase interstitial edema, and impair both systolic and diastolic function. A normal epicardial coronary angiogram does not exclude diffuse microvascular antibody injury.

Clinical clues that increase concern

- Unexpected ventricular dysfunction or reduced cardiac output
- Rising filling pressures or escalating inotropic support
- New atrial or ventricular arrhythmias
- Hemodynamic deterioration without a clear surgical explanation
- Rising or rebounding DSA
- Biopsy evidence of endothelial activation, microvascular inflammation, macrophages, or complement deposition

Why the Liver Can Protect the Heart

The liver is relatively resistant to antibody-mediated injury and has a uniquely large, immunologically active vascular bed. Because the liver and heart come from the same donor, the organs share many donor HLA targets. Once the liver is reperfused, it can reduce the freely circulating antibody burden before the heart is exposed. [1,4]

1 Antibody adsorption

The liver's extensive sinusoidal endothelial surface displays donor HLA. Recipient DSA bind those targets and leave the freely circulating antibody pool. This donor-specific adsorption is why clinicians often describe the liver as a living immunologic sponge. It is more specific than simple blood filtration.

2 Immune complex clearance

Kupffer cells and the hepatic reticuloendothelial system capture immune complexes, complement-coated material, and cellular debris. This clearance may further reduce active donor-directed antibody in the circulation.

3 Soluble donor HLA

The donor liver may release soluble HLA molecules that bind circulating DSA away from the heart. These soluble targets may contribute to the liver's protective effect, although their relative clinical importance remains incompletely defined.

4 Complement regulation

The liver synthesizes multiple complement proteins and regulatory factors. Hepatic uptake and regulation may modify complement activity after antibody binding. This mechanism remains biologically plausible but is less directly established than the rapid clinical fall in DSA after liver reperfusion.

5 Tolerogenic immune signaling

The hepatic immune environment limits unnecessary inflammation despite constant exposure to food antigens and microbial products from the portal circulation. Kupffer cells, sinusoidal endothelial cells, regulatory lymphocytes, and altered antigen presentation may reduce broader donor-directed immune activation. These effects may extend beyond antibody removal, but they do not create guaranteed or permanent tolerance.

Why the Liver Tolerates Antibodies Better

The liver is not immune to antibody-mediated rejection. Its architecture and immune biology, however, allow it to absorb a substantial antibody burden without developing the same immediate catastrophic microvascular dysfunction that may occur in the heart.

Feature	Liver	Heart
Vascular bed	Large sinusoidal surface creates extensive donor-HLA contact.	Dense coronary microcirculation must preserve uninterrupted myocardial perfusion.
Blood supply	Dual inflow from portal vein and hepatic artery.	Coronary circulation is the sole oxygen supply to working myocardium.
Immune-complex handling	Kupffer cells and reticuloendothelial pathways support clearance.	Microvascular deposition can rapidly impair perfusion.
Immune environment	Relatively tolerogenic with broad regulatory activity.	More vulnerable to complement-mediated endothelial injury.
Reserve	Substantial functional and regenerative reserve.	Diffuse injury can quickly reduce output and destabilize hemodynamics.

What HALT Is Designed to Accomplish

The goal is not to make DSA disappear forever. The immediate objective is to reduce antibody activity during the interval when the donor heart is most vulnerable to rapid endothelial binding and complement-mediated injury.

The donor liver takes the first and largest wave of antibody exposure.

The clinical evidence remains limited to selected patients and experienced centers. HALT requires coordinated surgical, immunologic, anesthesia, perfusion, and postoperative planning. It is not a general solution for sensitization in patients who do not otherwise require liver transplantation.

The HALT Sequence

Step	What happens	Clinical purpose
1 Identify risk	Define HLA antibodies, DSA, cPRA, virtual crossmatch, and physical crossmatch when indicated.	Characterize donor-specific risk before accepting and sequencing the organs.
2 Implant liver first	Reperfuse the donor liver while the donor heart remains preserved.	Expose the liver to the recipient's antibody burden before the heart.
3 Reassess	Repeat DSA or crossmatch testing according to the center's protocol and operative timeline.	Confirm that antibody activity has fallen and look for rebound.
4 Implant heart	Proceed with donor-heart implantation after the protective interval.	Reperfuse the heart into a less antibody-reactive circulation.

What may change after liver reperfusion

- DSA strength may fall rapidly, sometimes within minutes to hours in reported experience.
- A previously positive flow or cytotoxic crossmatch may weaken or convert.
- The decline may differ by antibody class, specificity, strength, and assay.
- Residual or rebounding antibody may still remain clinically important.

Interpret the laboratory result in context

Mean fluorescence intensity is semiquantitative and varies with assay conditions. A change in MFI does not automatically equal a proportional change in biologic risk. The histocompatibility laboratory and transplant team should interpret antibody specificity, dilution behavior, complement-binding data, crossmatch results, graft function, and the full clinical picture.

HALT Does Not Eliminate Rejection

HALT may markedly lower early antibody-mediated risk, but it does not establish complete or permanent immune tolerance. The recipient still requires center-specific induction therapy, maintenance immunosuppression, infection prevention, and structured surveillance.

Ongoing risks

- DSA rebound or persistent low-level DSA
- Development of de novo DSA
- Acute antibody-mediated rejection
- Acute cellular rejection
- Mixed cellular and antibody-mediated rejection
- Liver allograft cellular or antibody-mediated injury
- Cardiac allograft vasculopathy
- Infection, cytopenias, kidney injury, or medication toxicity related to immunosuppression

A positive DSA result is not a diagnosis by itself

DSA identifies immunologic risk or activity. A diagnosis of rejection requires integration with graft function, hemodynamics, echocardiography, biomarkers, pathology, and the clinical trajectory. Conversely, early antibody-mediated injury may begin before dramatic ventricular dysfunction becomes apparent. [2,3]

What the bedside clinician should communicate

- The direction and timing of the DSA trend
- Current biventricular function and cardiac-output trend
- Filling pressures, vasoactive and inotropic requirements, and rhythm changes
- Cardiac and liver laboratory trends
- Biopsy, echocardiography, imaging, and crossmatch findings
- Current immunosuppression and any missed, delayed, or poorly absorbed doses
- Competing explanations for graft dysfunction

Postoperative Cardiac Surveillance

Monitor for new or worsening evidence of cardiac allograft dysfunction:

- New ventricular dysfunction or reduced cardiac output
- Rising right- or left-sided filling pressures
- New atrial or ventricular arrhythmias
- Escalating inotropic or mechanical circulatory support
- Hemodynamic instability or impaired end-organ perfusion
- Rising troponin or natriuretic peptide trends when used by the center
- Abnormal endomyocardial biopsy findings

Endomyocardial biopsy may assess

- Acute cellular rejection
- Microvascular inflammation
- Endothelial activation or swelling
- Intravascular macrophages
- C4d or other complement deposition
- Pathologic features of antibody-mediated rejection

Postoperative Liver Surveillance

- AST, ALT, alkaline phosphatase, GGT, and bilirubin trends
- INR, glucose, lactate clearance, and other measures of synthetic or metabolic function
- Hepatic artery, portal vein, and hepatic venous flow when assessed
- Biliary complications
- Evidence of hepatic cellular or antibody-mediated rejection
- Hemodynamic and medication-related causes of liver-test abnormalities

Immunologic Surveillance

- Serial DSA measurements according to the center's schedule
- Changes in antibody strength, specificity, and class
- Recurrence or rebound of preformed DSA
- Appearance of de novo DSA
- Crossmatch results when clinically indicated
- Clinical and pathologic evidence of antibody-mediated injury

Bedside Warning

Antibody activity may precede obvious graft dysfunction. Escalate new graft concerns promptly when rising or rebounding DSA accompanies any of the following:

- Hemodynamic deterioration or increasing filling pressures
- Reduced cardiac output or new ventricular dysfunction
- Unexplained arrhythmias
- Increasing inotropic or mechanical-support requirements
- Biopsy evidence of endothelial or microvascular injury
- Concurrent deterioration in liver allograft function

Evaluate competing diagnoses at the same time

Category	Urgent considerations
Mechanical or surgical	Tamponade, hemorrhage, coronary compromise, inflow or outflow obstruction, vascular complication
Hemodynamic	Hypovolemia, RV failure, pulmonary hypertension, vasoplegia, uncontrolled hypertension
Allograft	Early graft dysfunction, AMR, cellular rejection, mixed rejection
Systemic or treatment related	Sepsis, hypoxemia, arrhythmia, medication toxicity, under-immunosuppression

Acute Care Atlas Bedside Checklist

Use this framework when presenting a postoperative HALT recipient or escalating concern. Center protocols remain authoritative.

Heart allograft

- What changed in ventricular function, output, filling pressures, rhythm, or support?
- Is the trajectory improving, stable, or worsening?
- Do biopsy, echocardiography, biomarkers, and hemodynamics tell the same story?

Liver allograft

- Are transaminases, bilirubin, INR, glucose, and lactate following the expected trajectory?
- Are hepatic artery, portal vein, and venous flows adequate when assessed?
- Could congestion, low flow, medication toxicity, or biliary disease explain the pattern?

Immunology and treatment

- What are the DSA specificity, class, strength, and trend?
- Was the sample obtained at the clinically intended time?
- Have immunosuppression doses been given, absorbed, and adjusted for organ function?
- Is infection risk changing the immunosuppression plan?

Escalation statement

A concise escalation should name the change, show the supporting trend, identify the immediate physiologic risk, and state what evaluation or intervention is needed now.

HALT lowers the initial antibody burden. Vigilant surveillance protects both allografts afterward.

Acute Care Atlas Takeaway

HALT is both a surgical sequence and an immunologic risk-reduction strategy. By transplanting and reperfusing the donor liver first, the team uses the liver's extensive endothelial surface and immune-complex handling to reduce circulating donor-specific antibodies. Additional complement-regulatory and tolerogenic mechanisms may contribute. The donor heart is then implanted into a circulation that is less capable of launching immediate antibody-mediated microvascular injury.

The liver meets the antibodies first so the heart does not have to.

Selected References

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Educational Use and Disclaimer

This guide is for clinician education and does not replace patient-specific evaluation, transplant-center protocols, pathology interpretation, histocompatibility expertise, or specialist consultation. Immunosuppression, DSA thresholds, biopsy schedules, crossmatch methods, and escalation pathways vary by center.

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