Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/25**
(See policy history boxes for previous effective dates)

Title: Transplant-Heart-Kidney (Combined)

Description/Background

Solid organ transplantation offers a treatment option for patients with different types of end-stage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life.[17,] Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by Organ Procurement and Transplantation Network (OPTN) and United Network of Organ Sharing (UNOS).

In 2019, Awad et al published a study regarding the number of individuals undergoing heart-kidney transplantation between June 1992 and December 2016, the number of patients undergoing heart and kidney transplantation (HKTx) increased, as well as the number of waitlisted patients for HKTx.[1] While on the waitlist, the 3-month mortality rate of HKTx-listed patients was observed to be 21% in dialysis-dependent patients and 7% in nondialysis-dependent patients with renal insufficiency. Analysis of the United Network for Organ Sharing (UNOS) registry showed similar mortality rates between heart transplantation (HTx)- and HKTx-listed patients, but the 5-year survival rates of HKTx recipients were higher than the survival rates of HTx recipients with renal insufficiency regardless of the pretransplant dialysis dependence status. Another analysis of the UNOS registry showed higher survival rates in HKTx recipients than in HTx recipients requiring pretransplant dialysis, and further analysis of the UNOS database provided an association between pre-HTx estimated glomerular filtration rate (GFR) and end-stage renal disease, kidney transplantation, and mortality for up to 10 years after HTx. A pre-HTx estimated GFR <60 mL/min per m^2 was associated with increased

mortality after HTx. Thus, lower GFR portended higher renal risks and mortality after isolated HTx.

These findings suggest that concomitant heart failure and renal insufficiency warrants consideration for HKTx without necessitating dialysis dependence. In patients with pre-HTx renal dysfunction with abnormal GFR, one also needs to consider the increased risk of end-stage renal disease following HTx because of the cumulative effects of calcineurin inhibitor nephrotoxicity and the attendant increase in post-HTx mortality if end-stage renal disease develops.[1]

Regulatory Status

N/A

Medical Policy Statement

Combined heart-kidney transplants have been clinically established. It may be considered a useful therapeutic procedure for carefully selected individuals when criteria are met.

Inclusionary and Exclusionary Guidelines

Inclusions:
Heart-kidney transplantation may be indicated in individuals who qualify for combined heart-kidney transplantation and have advanced irreversible heart and kidney disease.

Indications for combined heart-kidney transplant include but are not limited to progressive chronic heart/kidney disease unresponsive to other medical and surgical therapy. In general patients are selected for combined heart-kidney transplant if one or more of the following apply:

- End-stage heart and kidney disease not amenable to any other form of therapy;
- End stage heart disease and estimated glomerular filtration rate (eGFR) is 33 mL/minute or less, or preoperative evaluation of the kidney indicates the likelihood that the rate of progression of renal injury or dysfunction after single organ transplant is high.

Heart-kidney retransplantation after a failed primary heart-kidney transplant may be considered established in individuals who meet criteria for heart-kidney retransplantation.

Exclusions:

- Combined Heart-kidney transplantation is considered investigational in all other situations.

Potential Contraindications for Transplant/Retransplant:
Note: Final patient eligibility for transplant is subject to the judgment and discretion of the requesting transplant center.

Potential contraindications represent situations where proceeding with transplant is not advisable in the context of limited organ availability. Contraindications may evolve over time as transplant experience grows in the medical community. Clinical documentation supplied to the health plan should demonstrate that attending staff at the transplant center have considered all contraindications as part of their overall evaluation of potential organ transplant recipients and have decided to proceed.

- Known current malignancy, including metastatic cancer;
- Recent malignancy with moderate or high risk of recurrence;
- History of cancer with a moderate risk of recurrence;
- Untreated systemic infection making immunosuppression unsafe, including chronic infection;
- Other irreversible end-stage disease not attributed to heart or kidney disease;
- Systemic disease that could be exacerbated by immunosuppression;
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy.

All transplants must be prior authorized through the Human Organ Transplant Program.

The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation will be used as a reference for determining clinical suitability.

*Please note there are individual policies for each of these organs (heart transplant, kidney transplant) which contain more detailed information.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

33945 50360 50365

Other codes (investigational, not medically necessary, etc.):

N/A

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

COMBINED HEART-KIDNEY TRANSPLANTATION

The purpose of a combined heart-kidney transplantation for individuals who have indications for heart and kidney transplant is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICO** was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with indications for heart and kidney transplant.

Interventions

The therapy being considered is a combined heart-kidney transplantation.

Comparators

The following tools and practices are currently being used to make decisions about managing combined heart-kidney transplantation: medical management or single organ transplant.

Outcomes

The general outcomes of interest are OS and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections). Short-term follow-up ranges from immediate post-surgery to 30 days post transplantation; lifelong follow-up (out to 10 years or more given current survival data) is necessary due to ongoing immunosuppression and risk of graft failure.

Review of Evidence

Although in the past patients with end-stage heart failure and concurrent renal disease were excluded as candidates for heart transplantation, studies have shown combined heart and kidney transplantation has improved outcomes in a subset of patients that meet select criteria. Russo and colleagues' (2009) analysis of the UNOS database found that recipient survival with combined organ transplantation has increased when compared with heart transplantation alone when the eGFR at the time of listing was less than 33 mL/min.[2]

Multivariate Cox proportional hazards regression analysis was performed to identify Pre-transplantation recipient characteristics associated with improved long-term survival following HKT. Kaplan-Meier survival functions and Cox proportional hazards regression were used for time-to-event analysis. Using the relative risks calculated in regression analysis, weights were assigned for each risk factor, allowing for the construction of a risk score. Among heart transplant recipients, 264 (1.4%) underwent HKT. Factors associated with diminished survival included peripheral vascular disease, recipient age older than 65 years, nonischemic etiology of heart failure, dialysis dependence at the time of transplantation, and bridge to transplantation using a ventricular assist device. After stratification by risk score, 1-year survival was 93.2% and 61.9% in the lowest- and highest-risk HKT groups, respectively. Further stratification by estimated glomerular filtration rate (eGFR) was performed based on a previous study showing decreased survival of patients undergoing orthotopic heart

transplantation with a preoperative eGFR of less than 33 mL/min. Low-risk patients with an eGFR of less than 33 mL/min undergoing HKT constituted the only group that had significantly better survival compared with isolated patients undergoing orthotopic heart transplantation with eGFRs and risk scores in the same range (P=.006). The authors concluded that when patients were stratified by risk score and by diminished eGFR (< 33 mL/min), low-risk HKT recipients with a diminished eGFR had improved survival following HKT over isolated heart transplant recipients. Only low-risk patients with combined kidney failure (eGFR, < 33 mL/min) and heart failure seem to gain a survival benefit from HKT.

A longer- term analysis between April 1989 and November 2009 also supports combined HKT as a therapeutic option for a select group of recipients. Bruschi and colleagues (2010) studied nine patients who underwent combined simultaneous HKT.[3] Good cardiac function with low inotropic support occurred in all patients. Except for one patient, immediate diuresis from the transplant kidney took place. The exception was a 55 year old patient who received the organs from a 69 year old donor. Systemic multiorgan failure developed, and the patient died 41 days after the HKT. Otherwise, long-term results were satisfactory. As of 2010, only three patients have died. One was due to infection and multiorgan failure at 134 months, one due to a lung neoplasm after 6 years, and the last suffered a cerebral stroke 34 months after HKT. One patient needed renal replacement therapy after experiencing renal allograft failure secondary to hypertension and cyclosporine nephrotoxicity 10 years after transplantation.

As combined heart and kidney transplantation increased in frequency Ruzza et al (2013) noted that there were no guidelines to establish the indications, contraindications and sequence for this surgical procedure.[4] The authors reported on a single-center experience on 30 consecutive patients who underwent combined heart and kidney transplant in comparison with heart transplant alone. Patients had similar preoperative characteristics in both groups. Combined heart and kidney transplant is associated with the same long-term survival rate, low cellular rejection and antibody-mediated rejection rates when compared with heart transplant alone. The authors did not observe any difference in the outcomes related to preoperative patient characteristics. They suggested the staged surgical approach as the preferred method for transplant.

In 2017, Awad et al reported their clinical experience with combined heart and kidney transplantation (HKTx) over a 23-year time period.[5] From June 1992 to August 2015, the authors performed 83 combined HKTx procedures at their institution. They compared the more recent cohort of 53 HKTx recipients (group 2, March 2009 to August 2015) with the initial 30 previously reported HKTx recipients (group 1, June 1992 to February 2009). Pre-operative patient characteristics, peri-operative factors, and post-operative outcomes including survival were examined.

The baseline characteristics of the two groups were similar, except for a lower incidence of ethanol use and higher pre-operative left-ventricular ejection fraction, cardiac output, and cardiac index in group 2 when compared with group 1 (P = .007, .046, .037, respectively). The pump time was longer in group 2 compared with group 1 (153.30 ± 38.68 vs. 129.60 ± 37.60 minutes; P = .007), whereas the graft ischemic time was not significantly different between the groups, with a trend to a longer graft ischemic time in group 2 vs. group 1 (195.17 ± 45.06 vs. 178.07 ± 52.77 minutes; P = .056, respectively). The lengths of intensive care unit (ICU) and hospital stay were similar between the groups (P = .083 and .39, respectively). In addition, pre-operative and postoperative creatinine levels at peak, discharge, 1 year, and 5 years and the

number of people on post-operative dialysis were similar between the groups (P = .37, .75, .54, .87, .56, and P = .139, respectively). Overall survival was not significantly different between groups 2 and 1 for the first 5 years after transplant, with a trend toward higher survival in group 2 (P = .054). The authors concluded that in selected patients with co-existing heart and kidney failure, combined heart and kidney transplantation is safe to perform and has excellent outcomes.

Weng et al (2017) reported on pediatric patients with combined cardiac and renal failure.[6] Often, these patients develop human leukocyte antigen antibodies from their previous allografts and are therefore more difficult to re-transplant. The authors describe the largest case series of a predominantly sensitized pediatric HKTx with emphasis on medical management and patient outcomes. Demographics, clinical characteristics, antibody, and biopsy data were retrospectively collected from University of California, Los Angeles database and correlated with short- and long-term patient and allograft outcomes of all HKTx performed between 2002 and 2015. They identified seven pediatric patients who underwent HKTx at their center. Mean age at time of HKTx was 13.7 years and 85.7% were re-graft patients. 57.1% were sensitized with cPRA >50% and another 57.1% had preformed donor-specific antibody. Five-year renal allograft survival and patient survival was 85.7% for both endpoints. The remaining six patients were all alive (mean follow-up 78.5 months) with good kidney and heart function. HKTx in a population with increased immunological risk can be associated with good long-term outcomes and offers potential guidance to the pediatric transplant community where data are limited.

In 2018, Sharma et al reported details on what they believed to be the first combined heart-kidney transplant in a recipient of a previous sequential heart and kidney transplant.[7] Eight years after a combined heart and kidney transplant after initially receiving a sequential heart and kidney transplant, a 31-year-old man is doing extremely well, with no rejection episodes or significant complications after transplantation. The authors concluded that this case confirms that combined heart and kidney transplantation is a viable option for tackling the complex issue of graft failure in recipients of previous cardiac and renal grafts.

Reich et al (2018) reported on outcomes after HKTx vs. isolated heart transplant in patients age ≥65 years.[8] Between 2010 and 2015, 163 recipients ≥65 years of age were transplanted in a single center: 12 heart–kidney and 151 isolated heart transplants. Outcomes assessed were estimated glomerular filtration rate at 1, 6 and 12 months after transplant, the need for dialysis, 1-year survival, 1-year freedom from rejection, 1-year freedom from cardiac allograft vasculopathy and 1-year freedom from non-fatal major adverse cardiac events. Recipient ages were 67.8 ± 1.6 and 69.0 ± 2.8 years for heart–kidney transplant and isolated heart transplant, and pre-transplant estimated glomerular filtration rates were 26.6 ± 9.4 vs. 55.2 ± 18.9, respectively. At 1 month (66.3 ± 31.4 vs. 67.2 ± 28.0, P = 0.92), 6 months (68.1 ± 21.3 vs. 60.5 ± 19.6, P = 0.20) and 12 months (58.6 ± 21.5 vs. 52.4 ± 18.5, P = 0.27) post-transplant, estimated glomerular filtration rate was similar for heart–kidney transplant versus isolated heart transplant. There was a trend towards reduced 1-year freedom from temporary dialysis after HKTx relative to isolated heart transplant (75.0% vs. 90.4%, P = 0.06) without a difference in 1-year freedom from chronic dialysis (100% vs. 95.2%, P = 0.46). There were no differences in 1-year survival, 1-year freedom from any treated rejection, acute cellular rejection, antibody-mediated rejection, cardiac allograft vasculopathy and non-fatal major adverse cardiac events. The authors concluded that patients ≥65 years old with HKTx can achieve outcomes on part with heart transplant alone.

Most recently, Toinet et al (2019), assessed renal outcomes in HKTx to identify predictive factors for renal loss.[9] A retrospective study was conducted among 73 HKTx recipients: Donors' and recipients' records were reviewed to evaluate patients' and renal transplants' survival and their prognostic factors. The mean follow-up was 5.36 years. Renal primary non-function occurred in 2.7%, and complications Clavien IIIb or higher were observed in 67.1% including 16 (22%) postoperative deaths. Five-year overall survival and renal survival were 74.5% and 69.4%. Among survivors, seven returned to dialysis during follow-up. The postoperative use of ECMO (HR = 6.04, P = 0.006), dialysis (HR = 1.04/day, P = 0.022), and occurrence of complications (HR = 31.79, P = 0.022) were independent predictors of postoperative mortality but not the history of previous HTx or KTx nor renal function prior to transplantation. History of KTx (HR = 2.52, P = 0.026) and increased delay between the two transplantations (HR = 1.25/hour, P = 0.018) were associated with renal transplant failure. HKTx provides good renal transplant survival and function, among survivors. Early mortality rate of 22% underlines the need to identify perioperative risk factors that would lead to more judicious and responsible allocation of a scarce resource.

SUMMARY OF EVIDENCE

As consideration is given for non- renal solid organ transplants, the preoperative evaluation of the kidney must assess the likelihood of post-transplant function. If the post-transplant renal function is stage 4 or stage 5, or the primary renal disease is likely to rapidly progress shortly after transplant, then the patient should be considered for a combined organ transplant.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

No practice guidelines or position statements found addressing combined heart-kidney transplantation.

Ongoing Clinical Trials

There are no current clinical trials that may influence this review.

Government Regulations

National:

Cardiac transplantation is covered under Medicare when performed in a facility which is approved by Medicare as meeting institutional coverage criteria. (CMS Ruling 87-1.)

Local:

An LCD does not exist for a kidney transplant or combined heart-kidney transplant. Fees exist for renal allotransplantation procedure codes.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Transplant-Heart
- Transplant-Heart-Lung (Combined)
- Transplant-Heart-Kidney (Combined)
- Transplant-Islet Cell
- Transplant-Liver
- Transplant-Liver-Kidney Transplant (Combined)
- Transplant-Lung-Lobar Lung
- Transplant-Pancreas
- Transplant-Small Bowel-Liver/Multivisceral (Combined)
- Transplant-Small Bowel Transplant (Isolated)

References

1. Awad MA, Czer LS, Emerson D, et al. Combined heart and kidney transplantation: clinical experience in 100 consecutive patients. J Am Heart Assoc. 2019;e010570.
2. Russo MJ, Rana A, Chen JM, Hong KN, et al. Pretransplantation patient characteristics and survival following combined heart and kidney transplantation. Arch Surg. 2009;144(3):241-246.
3. Bruschi G, Botta L, Colombo T, et al. Combined heart and kidney transplantation: long-term analysis of renal function and major adverse events at 20 years. Transplant Proc. 2010;42(4):1283-1285.
4. Ruzza A, Czer LS, Trento A and Esmailian Fardad. Combined heart and kidney transplantation: what is the appropriate surgical sequence? Interactive CardioVascular and Thoracic Surg. 2013;416-418.
5. Awad MA, Czer LS, Esmailian F, Jordan S, et al. Combined heart and kidney transplantation: a 23-year experience. Transplant Proc. 2017;49(2):348-353.
6. Weng PL, Alejos JC, Halnon N, et al. Long-term outcomes of simultaneous heart and kidney transplantation in pediatric recipients. Pediatr Transplant. 2017;21(7):PMID 28727227.
7. Sharma M, Anthony C, Hayward C, et al. Life-saving combined heart-kidney transplantation in previous sequential heart and kidney transplant recipient. Eur J Case Rep Intern Med. 2018;5(8):000924.
8. Reich H, Dimbil S, Levine R, Megna D, et al. Dual-organ transplantation in older recipients: outcomes after heart-kidney transplant versus isolated heart transplant in patients age ≥65 years. Interactive CardioVascular and Thoracic Surg. 2019;28(1):45-51.
9. Toinet T, Dominique I, Cholley I, et al. Renal outcome after simultaneous heart and kidney transplantation. Clin Transplant. 2019;e13615. PMID:31215696.
10. Gill J, Shah T, Hristea I, et al. Outcomes of simultaneous heart-kidney transplant in the US: a retrospective analysis using OPTN/UNOS data. Am J Transplant. 2009;8(4):844-852.

11. Schaffer JM, Chiu P, Singh SK, et al. Heart and combined heart-kidney transplantation in patients with concomitant renal insufficiency and end-stage heart failure. Am J Transplant. 2014;14(2):384-396.
12. Trachiotis GD, Vega JD, Johnston TS, et al. Ten-year follow-up in patients with combined heart and kidney transplantation. J Thorac Cardovas Surg. 2003;126:2065-2071.
13. Pham MX. Prognosis after cardiac transplantation in adults. 2019. Available at: www.uptodate.com. Accessed August 2019. In supplemental documents folder.
14. Kobashigawa J, Dadhania DM, Farr M, Tang WHW, et al. Consensus conference on heart-kidney transplantation. AM J Transplant. 2021; 21:2459-2467.
15. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. Transplantation. 2020; 104:S1-S103.
16. Improving Global Outcomes (KDIGO) Kidney Transplant Candidate Work Group. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. Transplantation. 2020;104: S1–S103.
17. Black CK, Termanini KM, Aguirre O, et al. Solid organ transplantation in the 21 st century. Ann Transl Med. Oct 2018; 6(20): 409. PMID 30498736

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2025, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
1/1/20	11/26/19		Joint policy established
1/1/21	10/20/20		Routine policy maintenance, no change in policy status.
1/1/22	10/19/21		Routine policy maintenance, no change in policy status.
1/1/23	10/18/22		Routine policy maintenance, no change in policy status.
1/1/24	10/25/23		Added language to inclusion section. Title changed to start with "Transplant." Routine policy maintenance, no change in policy status. Added reference #14 & 15. Vendor managed: N/A (ds)
5/1/24	3/8/24		Routine review, referenced the KDIGO guidelines, guidelines also mentioned in inclusion/exclusion section. Title changed to Transplant-Heart-Kidney (Combined). Policy status unchanged. Vendor managed: N/A (ds)
5/1/25	2/18/25		Language revision to MPS, added language for retransplantation to inclusions. Routine policy maintenance. Vendor managed: N/A (ds)

Next Review Date: 1st Qtr. 2026

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN:	Revised:
BCBSM:	Revised:

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: TRANSPLANT-HEART-KIDNEY (COMBINED)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered per policy
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.