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MATCH
Management of Post-Transplant Infections in Collaborating Hospitals

Evaluation of MATCH: an Electronic Individual Patient-Focused Management System Aimed at Preventing Cytomegalovirus Disease Following Solid Organ Transplantation

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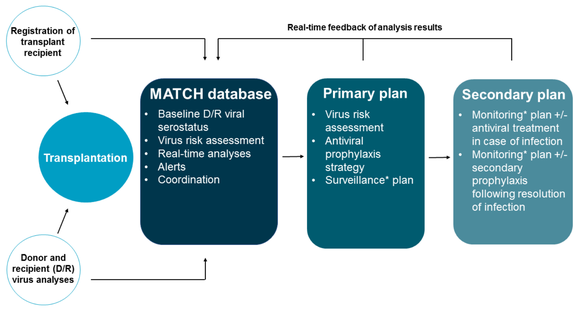
BACKGROUND

- Cytomegalovirus (CMV) infection is common among solid organ transplant (SOT) recipients and may cause CMV disease, if not promptly treated[1,2].
- Increasing viral load at the time of diagnosis of CMV DNAemia is a risk factor for CMV disease, however CMV disease may occur even at very low viral load, particularly in lung transplant recipients[3].
- Strategies to prevent CMV disease include chemoprophylaxis and pre-emptive monitoring and treatment of emerging subclinical infection. To optimize the implementation of these strategies as part of routine care, we developed and implemented a proactive and patient-tailored CMV management system for SOT patients (the MATCH program) in our center.
- Two key performance characteristics of success of MATCH are diagnosing CMV at low viral load and avoiding CMV disease at diagnosis; these characteristics are assessed here before (2007-2010), during (2011-2012) and after (2013-2015) the implementation of the MATCH program.

METHODS

- In MATCH, SOT recipients follow a personalized, yet standardized, plan for monitoring, prophylaxis and preemptive therapy depending on underlying risk for CMV infection (**Figure 1**).
- CMV infection is defined as two consecutive plasma CMV PCR ≥273 IU/mL taken ≤14 days of each other, or one CMV PCR ≥2730 IU/mL.
- The plan is composed in accordance with the recipient's a priori risk as to CMV IgG serostatus and is continually updated during the post-transplant course according to the patient's current situation.
- Each individual patient plan is produced and implemented by a rule-based artificial intelligence (AI) platform, harvesting relevant real-time data from electronic medical records.
- Plans and revisions are created via predefined algorithms.
- Alerts are automatically generated if samples for CMV PCR are not collected according to the plan or if CMV DNAemia is detected.
- Prior to its implementation, prevention of CMV disease was left at the discretion of the individual physician.

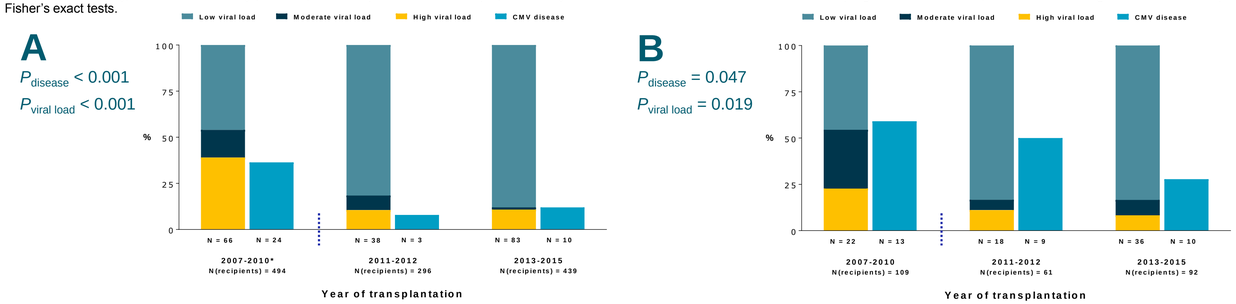
Figure 1. Principle features of the MATCH program.



TRANSPLANTATION AND MATCH DATABASE: Prior to transplantation, the recipient and donor are registered in the MATCH database which has real-time interface with hospital laboratory databases. Via this interface, serologic tests of both donor and recipient are automatically downloaded real-time to the database.
PRIMARY PLAN: Within one week after transplantation, a primary plan is generated which includes three components: 1) a virus risk assessment of viral infections according to the baseline D/R IgG serostatus, 2) a suggested antiviral prophylaxis strategy according to transplant type and risk assessment and 3) a surveillance plan. The two surveillance approaches utilized in the MATCH program consist of *surveillance after prophylaxis* (termed "hybrid approach" in prior guidelines) and *preemptive therapy*.
FEEDBACK OF ANALYSES: All laboratory analyses performed as part of the surveillance and monitoring plans are fed back to the MATCH database and generates alerts in case of abnormal analysis results (e.g. positive CMV PCR) and missed planned analyses.
SECONDARY PLAN: Secondary plans are generated in accordance with the individual recipient's post-transplant course (e.g. CMV infection). All recipients are followed for one year after transplantation.

***Surveillance:** patient at risk, but no evidence of an event or biomarker detection[1].
Monitoring: the patient has an event or a detected biomarker[1].

Figure 2. CMV disease at time of diagnosis of first CMV infection among recipients who developed CMV infection within the first year of transplantation before, during and after implementation of the MATCH program. Proportion with CMV disease among non-lung transplant recipients (**Panel A**) and lung transplant recipients (**Panel B**) who developed CMV infection within the first year of transplantation is illustrated by the light blue columns. The multi-coloured columns illustrate the first episode of CMV infection within the first year of transplantation by the proportion with high viral load (>27,300 IU/mL), moderate viral load (9,100 - 27,300 IU/mL) and low viral load (<9,100 IU/mL). The dotted blue lines indicate when the MATCH program was introduced, and *P* values were generated from chi-square and Fisher's exact tests.



* Due to inadequate data in the medical records we were unable to assess CMV disease in four patients with CMV infection in this time period.

Table 1. Characteristics of SOT recipients with a first episode of CMV infection within the first year of transplantation before, during and after implementation of the MATCH-programme.

Year of transplantation	2007-2010 (before implementation)	2011-2012 (during implementation)	2013-2015 (after implementation)
Recipients with a first episode of CMV infection, N(% of total no. of SOT)	88 (14.6)	56 (15.7)	119 (22.4)
Sex, N(%)			
Male	60 (68.2)	28 (50.0)	69 (58.0)
Female	28 (31.8)	28 (50.0)	50 (42.0)
Median age at transplantation (IQR), years	52 (38-59)	53 (41-59)	49 (38-58)
Transplant type, N(%)			
Heart	3 (3.4)	3 (5.4)	6 (5.0)
Kidney	43 (48.9)	25 (44.6)	41 (34.5)
Kidney-Pancreas	0	0	2 (1.7)
Liver	20 (22.7)	10 (17.9)	34 (28.6)
Lung	22 (25.0)	18 (32.1)	36 (30.3)
Donor/recipient CMV IgG serostatus at transplantation, N(%)			
D+/R-	25 (28.4)	27 (48.2)	53 (44.5)
D+/R+	23 (26.2)	22 (39.3)	44 (37.0)
D-/R+	3 (3.4)	3 (5.4)	17 (14.3)
D-/R-	1 (1.1)	0	3 (2.5)
Unknown	36 (40.9)	4 (7.1)	2 (1.7)
Median viral load of the first positive CMV PCR (IQR), IU/mL	11,421 (2,821 - 55,283)	637 (328 - 3,822)	637 (273 - 2,002)

RESULTS

- A total of 603, 357, and 531 patients received a SOT before, during and after implementation of MATCH, resp., of whom 88 (14.6%), 56 (15.7%) and 119 (22.4%) developed CMV infection within the first year of transplantation (**Table 1**).
- Among those transplanted, risk of CMV disease decreased over time for non-lung transplant patients ($P = 0.005$) but not for lung-transplant patients ($P = 0.77$), reflecting that CMV disease may present itself frequently in lung transplant patients despite low DNAemia[3].
- Among those with CMV infection, the proportion with high diagnostic viral load and the proportion presenting with CMV disease decreased over time ($P < 0.05$) (**Figure 2**).
- Residual risk of presenting with high CMV viral load and/or disease after implementation of MATCH mostly reflects non-compliance with recommendations (e.g. weekly screening is recommended but among those presenting with disease, ≤20% had been screened for CMV DNAemia within two weeks of diagnosis in all three calendar periods).

CONCLUSIONS

- The implementation of a rule-based AI platform guiding routine prevention of CMV disease among SOT recipients was associated with improved CMV-specific outcome, indicating its ability to identify the CMV infection sooner after onset and before causing disease.
- Continued focus on optimizing compliance with the MATCH program is expected to cause further reduction in risk of CMV disease.

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