

Healthcare professionals' perspective on the acceptance of gene therapy



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Recent seminal studies showed the ability of cardiac adeno-associated viral (AAV) gene therapy to induce plakophilin-2 (*PKP2*) and myosin-binding protein C (*MYBPC3*) gene expression, improving the prognosis of individuals affected by arrhythmogenic right ventricular cardiomyopathy with *PKP2* haploinsufficiency (present in ~50%–60% of arrhythmogenic right ventricular cardiomyopathy patients) and *MYBPC3*-associated hypertrophic cardiomyopathy, respectively.^{1–3} These promising results indicate that we are getting closer to true prevention or definitive treatment in genetically determined heart disease, which may cause life-threatening ventricular arrhythmias and/or heart failure.⁴ As fatal events may occur early in the course of these diseases, development of potentially curative treatment is of particular interest.

However, in our experience both patients and healthcare professionals look at gene therapy as an “unknown” treatment modality, which could inadvertently lead to its rejection as a therapeutic option.⁵ In this study, we aimed to (1) provide insights into the perceptions of healthcare professionals towards gene therapy as treatment for cardiomyopathy; and (2) explore the route to implementation of gene therapy in clinical care.

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KEY FINDINGS

- A trade-off between conceived risks and benefits drives healthcare professionals' attitudes toward gene therapy.
- All interviewed healthcare professionals considered cardiac gene therapy as a viable treatment option provided that it is proven safe in patients.
- Important themes that will improve acceptance of gene therapy include (1) expansion of knowledge, (2) transparent communication about its working mechanism and risks/benefits, (3) concentration of care in expertise centers, (4) designing treatment protocols and guidelines, and (5) performing health technology assessment.
- Active exploration of the road from bench to bedside is warranted to ensure implementation of this promising treatment option in clinical practice.

We conducted in-depth semi-structured interviews (mean duration 42 ± 6 minutes) among 13 Dutch healthcare professionals who are active in the field of cardiology (6 physicians, 4 nurses, and 3 researchers from 2 academic medical centers with cardiogenetic expertise [$n = 8$] and 2 community hospitals without cardiogenetic expertise [$n = 5$]) in April and May 2023. Transcripts were analyzed thematically and both within-case analysis and between-case analysis was

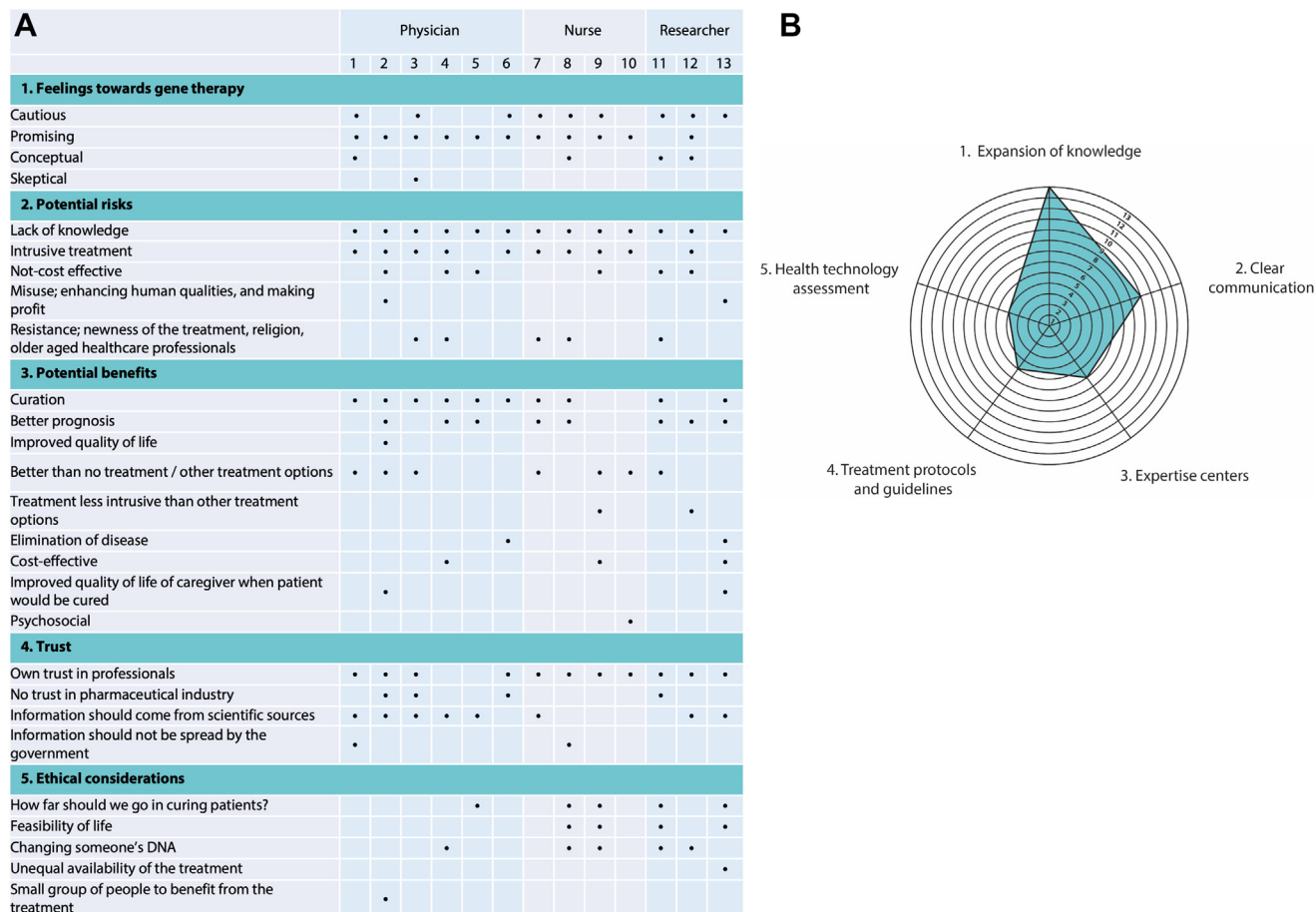


Figure 1 (A) Healthcare professionals’ perceptions stratified by profession on acceptance/rejection of gene therapy, categorized into bold aggregate dimensions with second-order themes as subcategories. (B) Healthcare professionals’ proposed strategy for implementing cardiac gene therapy. Themes were proposed respectively by the amount of 13, 9, 6, 5, and 4 healthcare professionals.

performed. We started with open coding, which formed the basis for development of second-order themes and aggregate dimensions (Figure 1A). All healthcare professionals considered cardiac gene therapy as a viable treatment option and said that they would potentially accept the treatment on the condition of its proven safety in patients. Balancing the trade-off between conceived risks and benefits, which appeared paramount in their decision-making process, was complicated by uncertainty attributed to the “unknown” aspect of the treatment. Higher trust in information sources made healthcare professionals more likely to accept the treatment. However, concerns persisted regarding potential risks, unidentified adverse effects, and misuse when utilized for enhancing human qualities and/or making profit rather than curing disease. Physicians expressed optimism towards gene therapy (“hopeful” or “revolutionary”), while nurses and researchers were more cautious (“scary” or “hesitant”). Also, ethical concerns were raised (“how far should we go to treat disease?”; “we should accept that life is finite”) including the desirability of altering human genetics (meaning “changing someone’s DNA and thus someone’s core”).

Figure 1B shows a summary of the healthcare professionals’ views on the necessary steps prior the gene therapy implementation in clinical practice: (1) expansion of knowledge regarding the safety, risks, long-term side effects, and efficacy of gene therapy; (2) clear and transparent communication about the working mechanism and risks/benefits of gene therapy to healthcare professionals, patients, and the general public; (3) concentration of care in expertise centers to enable fast sharing of experience and rapid knowledge improvement; (4) designing treatment protocols and guidelines on patient selection (especially on who and when to treat) and standardized follow-up to provide guidance in clinical practice; and (5) performing health technology assessments including a cost-effectiveness analysis comparing costs of gene therapy with conventional treatments and number needed to treat. All these steps aim to reduce the unfamiliarity regarding gene therapy and provide a solid foundation for decision-making regarding the treatment’s acceptability and potential implementation.

In conclusion, cardiac gene therapy emerges as promising treatment which enables favorable cardiac

remodeling or prevention of disease onset for genetic heart diseases. Our study (although relatively small) shows that its acceptance among healthcare professionals remains work in progress. Further research should be conducted in larger settings in which we may be able to learn from other fields in which gene therapy is already employed. Importantly, the patient's perspective should be obtained. Now is the time to further explore the road from bench to bedside to ensure implementation of a highly promising and viable treatment option for patients affected by genetically determined heart diseases.

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