Redesigning cardiovascular healthcare: patient and professional perspectives on value

Hilt, A.D.

CHAPTER VII

DEVELOPMENT OF A PATIENT-ORIENTED HOLOLENS APPLICATION TO ILLUSTRATE THE FUNCTION OF MEDICATION AFTER MYOCARDIAL INFARCTION

Alexander D. Hilt, MD; Beerend P. Hierck, MD, PhD; Joep Eijkenduijn, MSc;
Fons J. Wesselius, MSc; Armagan Albayrak, MEng, PhD; Marijke Melles, MEng, PhD;
Martin J. Schalij, MD, PhD; Roderick W.C. Scherptong, MD, PhD.

Published
European Heart Journal - Digital Health,
Volume 2, Issue 3, September 2021, Pages 511–520

Abstract

Background

Statin treatment is one of the hallmarks of secondary prevention after myocardial infarction. Adherence to statins tends to be difficult and can be improved by patient education. Novel technologies such as Mixed Reality (MR) expand the possibilities to support this process.

Objective

To assess if an MR medication-application supports patient education focused on function of statins after myocardial infarction.

Methods

A human centered design-approach was used to develop an MR statin tool for Microsoft HoloLens™. Twenty two myocardial infarction patients were enrolled; twelve tested the application, ten patients were controls. Clinical, demographic, and qualitative data were obtained. All patients performed a test on statin knowledge. To test if patients with a higher tendency to become involved in virtual environments affected test outcome in the intervention group, validated Presence- and Immersive Tendency Questionnaires (PQ and ITQ) were used.

Results

Twenty two myocardial infarction patients (STEMI, 18/22, 82%) completed the study. Ten out of twelve (83%) patients in the intervention group improved their statin knowledge by using the MR application (median 8 points, IQR 8). Test improvement was mainly the result of increased understanding of statin mechanisms in the body and secondary preventive effects.

A high tendency to get involved and focused in virtual environments was moderately positive correlated with better test improvement ($r=0.57$, $P<0.05$) The median post- test score in the control group was poor (median 6 points, IQR 4).

Conclusions

An MR statin education application can be applied effectively in myocardial infarction patients to explain statin function and importance.

List of abbreviations

ADL	Activities of Daily Living
AR	Augmented Reality
DT	Design Thinking
ITQ	Immersive Tendencies Questionnaire
IQR	Inter Quartile Range
MI	Myocardial Infarction
MR	Mixed Reality
NSTEMI	Non ST-Elevation Myocardial Infarction
PQ	Presence Questionnaire
STEMI	ST- Elevation Myocardial Infarction

VII

Introduction

Global mortality and morbidity due to coronary artery disease is high; roughly 85% of all cardiovascular deaths is due to myocardial infarction alone(1). Hypercholesterolemia is an important risk factor in the development of coronary atherosclerosis, and an important determinant of recurrent myocardial infarction(2). Statin treatment is the hallmark of secondary cardiovascular disease prevention, however statin *adherence* among patients remains a challenge(3, 4). Non-adherence to statins increases the risk of new cardiovascular events drastically(5).

Statin non-adherence is commonly related to both unintentional (practical) and intentional (motivational) barriers(4, 6, 7). Sociodemographic patient factors, negative media coverage, and the nocebo effect are contemporary factors that negatively affect statin adherence(8, 9). To improve statin adherence, patient education is essential(10). Visual anatomy or pathophysiology models can support healthcare professionals in this process(11-14).

Visual education of myocardial infarction patients is commonly done via conventional methods in the outpatient setting, such as booklets or online videos. Nonetheless, improvements regarding visual education have been made over the years (15, 16).

With rapid development of new technologies such as augmented- and mixed reality (AR/MR)(17, 18), options in visual patient education are expanding(19, 20). MR creates interactive digital three-dimensional (3D) holographic projections, overlaying virtual objects on the real-world environment. While augmented reality only overlays objects, MR anchors virtual objects to the real world, fostering interaction between user and virtual object. For medical students, MR technology supports education and improves learning(18, 21). Papers with a focus on patient education with extended realities such as virtual- or augmented reality become more present in daily clinical care(22-24). However, education through MR is scarce and non-existent in clinical cardiology to date. Interestingly, a recent study found that statin education might be a feasible target for an MR application in myocardial infarction patients(25).

The aim of the present study was to develop and test the feasibility of an MR statin education application in the outpatient setting of myocardial infarction patients. It was hypothesized that an interactive MR model is effective in transferring knowledge about the function of statins after myocardial infarction. Furthermore, it was hypothesized that patients who become easily focused and immersed within virtual environments would benefit the most from this technology(26).

Methods

This non-randomized controlled observational study is part of a project investigating the clinical application of MR in myocardial infarction patients. Ethical approval for the project was obtained through the local medical ethics committee of Leiden University Medical Center (protocol number P18.132).

General Study Design

An overview of the study design is presented in figure 1. Twenty two patients who visited the dedicated myocardial infarction outpatient clinic were asked to participate in the study; twelve underwent the intervention, ten patients were used as a control group.

For the intervention group, inclusion criteria were; patients, of 18 years or older i) who had either a ST-elevation myocardial infarction (STEMI) or non ST-elevation myocardial infarction (NSTEMI) and were treated in our center, ii) were one month after initial myocardial infarction, and iii) without impaired vision or hearing which could interfere with using the application. Patients were excluded if they had participated in the previous study in our center concerning MR use in the outpatient setting(25). Informed consent was collected prior to study participation. Demographic data such as age, gender and occupation were collected. Initial diagnosis (STEMI/NSTEMI), pharmaceutical data such as type of statin used, dosage and possible side effects were collected from the electronic medical record. An MR model was shown to all patients in the intervention group in the outpatient clinic via a first generation Microsoft™ HoloLens™. The procedure was guided by a research assistant. Patients were instructed to follow HoloLens audio cues and use all functionalities of the application for one hour. General comments on application-use were simultaneously collected by the assistant. Patients in the intervention group filled out a pre-test on statin knowledge and the Immersive Tendency Questionnaire (ITQ, see below) before using the MR model. The pre-test score was deemed 'test-score after conventional education' (T=0, figure 1). The ITQ assesses if a patient has either a high or low tendency to become focused in virtual environments. After using the model, the Presence Questionnaire (PQ) was filled out; this assesses if the MR model generates high levels of focus for what is shown (statin function). The post-test (T=1, figure 1) consisted of a telephone interview with a focus on statin knowledge.

A control group was used to determine the general effect of conventional statin education via a nurse on statin knowledge in myocardial infarction patients. For the control group, inclusion criteria were: patients, of 18 years or older i) who had either a STEMI or NSTEMI and were treated in our center, ii) were discharged one month prior to study begin or longer and had received conventional education from a specialized nurse at hospital discharge and during outpatient follow-up.

All control patients were naïve for the purpose of the study and completed the post-test via telephone at either 1, 6 or 12 months after discharge. This post- test score (T=0, figure 1) was deemed 'test score after conventional education'. Patients were excluded if they had participated in the previous study in our center concerning MR use in the outpatient setting(25).

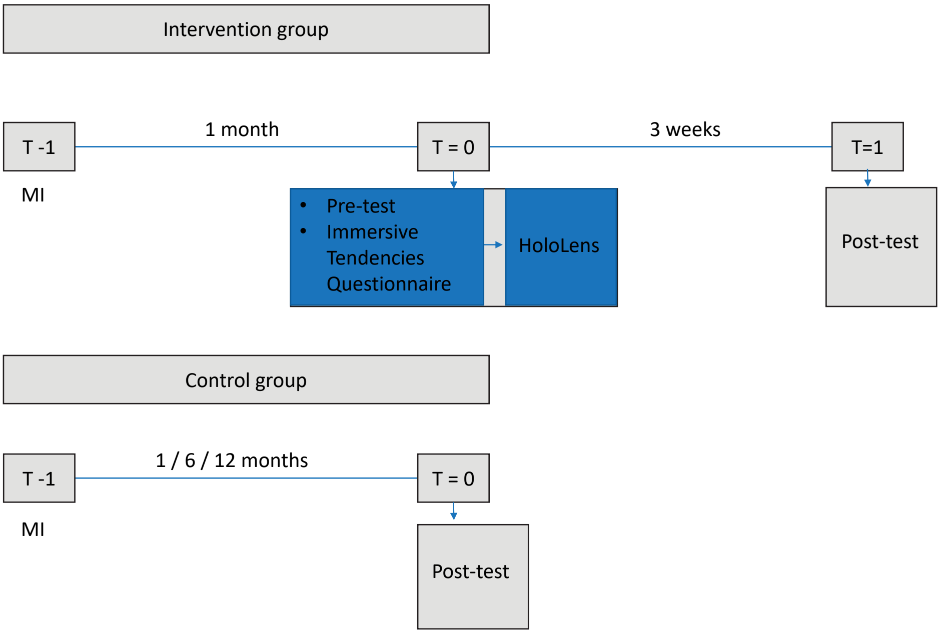

Figure 1. Study overview (intervention- and control group).

Caption: intervention group patients completed a pre-test on statin knowledge after conventional education (T=0) and a questionnaire on immersive tendencies before using the HoloLens application. After using the HoloLens, a presence questionnaire was filled out. Three weeks later, all patients completed the post-test on statin knowledge via phone. All control group patients underwent the post-test via telephone, after they had received the conventional education (T=0) via a specialized nurse, 1, 6 or 12 months after their initial myocardial infarction.

Development of the Mixed Reality Model

The 'double-diamond' human centered design approach, as introduced by the British Design Council in 2005, was used to create the application(27-29). This approach maps the divergent and convergent stages of a design process, showing different modes of design thinking in a structured manner (Figure 2A-D). The first phase (Figure 2A) comprised the preceding study and concluded that statin therapy might be a feasible target for an MR application (25). For the next phase, a correct anatomical 3D heart model (Figure 1B) was obtained online to develop further into a first prototype (Figure 2C). The final phase (Figure 2D) concerns the development of a commercially available product and, as such is not part of the current study. For prototype development, in addition to the patient perspective(25), interviews with two specialized nurses and two cardiologists frequently attending myocardial infarction patients in the outpatient setting of our hospital, were used to define the essential educational topics regarding statin function to be shown in the model.

This concluded that, to understand statin function, the model should contain animations of; i) cholesterol particles in the blood, ii) atherosclerosis in the coronary vessels, iii) an effect of cholesterol on atherosclerosis, and iv) an effect of statins on cholesterol particles and thus atherosclerosis. Additionally, the effect of atherosclerosis on blood flow and an effect of blood flow on oxygen distribution in the heart was incorporated.

The prototype was built using a set of tools to create an MR model in Blender 2.79, Microsoft ™ Visual studio community 2017, Mixed Reality Toolkit (Version 2017.4.0.0) and Unity, a game development tool, in which 3D or 2D models are programmed using C# or JavaScript(30). The model was stored on a first generation Microsoft™ HoloLens™, Development Edition with a Windows 10 update (Version 10.0.17763.134). With the Microsoft™ HoloLens™, interactive 3D holographic models can be freely handled via hand gestures. Additionally, within the prototype, the user could activate different animations such as ‘show cholesterol particles’, ‘blood flow’ or ‘show atherosclerosis’ in the coronary vessels. When ‘statin function’ was activated, the amount of cholesterol particles would decrease and the severity of atherosclerosis would decrease. Eight educational audio cues were recorded and build into the model (appendix 1). The final version of the prototype (C) was used in the present study. A video of the model is added as a supplementary file (video appendix 1).

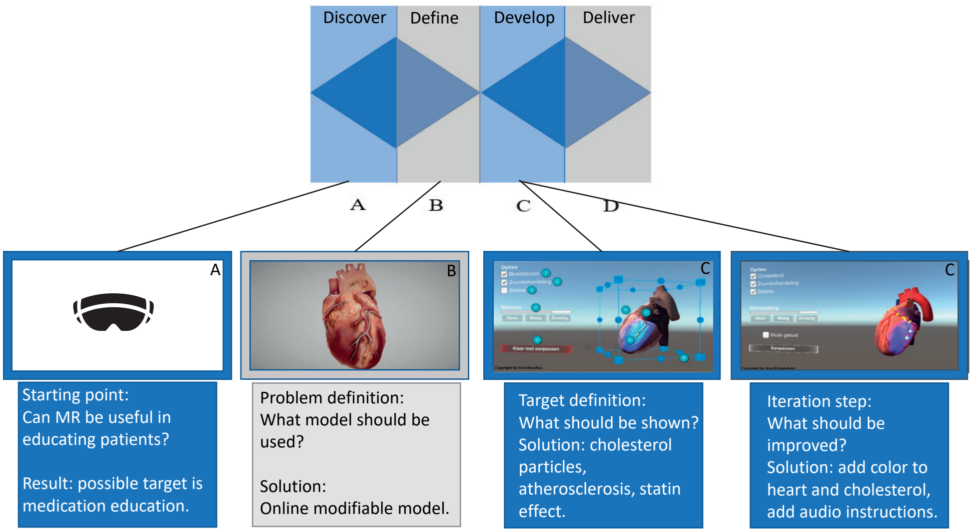

Figure 2. Double Diamond method.

Caption: the double diamond design approach is a standardized method to assess a problem through diverse divergent- and convergent steps (A – C) and ultimately deliver a solution (D).

Assessment of Knowledge on Statin Function

Patient's understanding of statins was tested via a pre- and post-test. The pre-test consisted of five questions regarding statin-effects in the body: i) 'what substances in the body are affected by statins?', ii) 'in what part of the body do statins work/have their function?', iii) 'which side effects do statins commonly give?', iv) 'how long do statins stay active in the body?' and v) 'how fast do statins work in the body?'. Correct answers, or answers containing elements as 'cholesterol/LDL', 'lower cholesterol and/or prevent new cardiovascular events', 'muscular- and gastro intestinal complaints', 'a month' and 'within one or two hours' were rewarded 10 points maximally (appendix 3).

The post-test consisted of one open question for which, identically, 50 points could be scored maximally: 'Could you elaborate in your own words, what the function of statins is in the body and what negative effects can occur because of it'. Each correct part of the answer was rewarded with 10 points, equal to the pre-test (appendix 3). Both pre- and post-test were identical regarding contents.

Control patients only took the post-test. All test outcomes were separately scored by researchers ADH and JE and compared afterwards to reach consensus. The test improvement (difference in pre- and post- test score) was calculated for each patient.

Measurement of Presence and Immersive tendencies

Patients' personal tendency to become focused and immersed within the MR model and its visualizations, were investigated via validated Immersive Tendency-, and Presence Questionnaires (ITQ and PQ)(26). Both questionnaires are used to characterize the likelihood of subjects to become fully focused within a virtual environment(31, 32). The ITQ quantifies a person's individual tendency to become focused in virtual environments.

High cumulative scores (minimum 18 – maximum 126) represent a high tendency to become easily immersed in virtual environments. The PQ quantifies the amount of focus a person experiences on objects or tasks, *generated by* a digital application. The higher the cumulative score (minimum 22 - maximum 154), the higher the focus for the objects shown in the MR model (see appendix 2).

For this study, two questions regarding haptic feedback were removed from the original PQ as this feature was not present in our application. Both ITQ and PQ scores were compared and correlated with the changes in test results, to determine if these device and patient characteristics showed a relationship with test improvement.

Analysis

Non-normally distributed ITQ, PQ and pre- and post-test numerical data are presented as absolute numbers with medians and Inter Quartile Range (IQR). A Spearman Rank test for correlation was calculated for non-normally distributed data; correlation coefficients (r) between Immersive Tendency and test improvement, as well as Presence and test improvement were calculated. Content analysis was used to structure all qualitative data; authors ADH and JE categorized responses to major themes that emerged from the data. For analysis, SPSS Statistics for Windows, version 23.0 (IBM Corp), was used. A *P*-value of less than .05 was considered significant.

Results

Study Population - Demographics

Twenty two myocardial infarction patients were enrolled in the study; the intervention group consisted of 9/12 (75%) males. Median age was 60.0 (IQR 9,5) years. The control group consisted of 5/10 (50%) males, median ages was 63.0 (IQR 5) years. All patients in the intervention group were tested at one month after initial myocardial infarction. Patients in the control group, were recruited at variable time-points after the initial MI: 1 month (n=3), 6 months (n=3) and 12 months (n=4). The majority of patients (18/22, 82%) suffered initially ST-elevation myocardial infarction (STEMI) (table 1 and 2).

Most patients used Atorvastatin 40 milligrams once daily (16/22, 73%), with an average duration of 1,5 (SD 0.6) years since the initial myocardial infarction. Muscle cramps (7/22, 32%) and fatigue (2/22, 10%) were frequent encountered side effects. Three (3/22, 14%) patients had personally terminated statin therapy during outpatient follow up; 19/22 (86%) of patients self-reported full adherence to statins (table 1 and 2). In comparison to the intervention group, the control group consisted of slightly more; NSTEMI patients (20% vs 17%, p=.82), females (50% vs 25%, p=.37) and therapeutically adherent patients (100% vs 75%, p=0.08) with a higher median age (63 years, IQR 5 vs 60 years, IQR 5, p=.1). These differences were however not statistically different.

Table 1. Demographics (intervention group)

Patient	Age(y)	Sex	Education	Type of MI	Statin	Daily Dosage	Side effects	Adherence
P001	60	F	Middle school	STEMI	Simvastatin	40	None	Complete
P002	39	M	BSc	STEMI	Atorvastatin	40	None	Complete
P003	62	M	MSc	STEMI	Atorvastatin	40	None	Complete
P004	72	M	Msc	STEMI	Atorvastatin	20	Muscle Cramp	Complete
P005	60	M	Highschool	STEMI	Atorvastatin	40	Fatigue, GI-cramps	Complete
P006	55	M	Highschool	STEMI	Atorvastatin	40	Fatigue	Complete
P007	50	M	Middle school	NSTEMI	Rosuvastatin	5	Muscle Cramp	Incomplete*
P008	60	F	Highschool	STEMI	Rosuvastatin	5	Muscle Cramp	Incomplete*
P009	67	F	Highschool	NSTEMI	Atorvastatin	40	None	Incomplete*
P010	44	M	Middle school	STEMI	Atorvastatin	40	Muscle Cramps	Complete
P011	58	M	BSc	STEMI	Rosuvastatin	10	Tingling sensation	Complete
P012	72	M	MSc	STEMI	Atorvastatin	40	None	Complete

BSc= bachelor of science; F= female; GI= gastrointestinal; M= male; MG= milligram; MI = myocardial infarction; NSTEMI = non ST elevation myocardial infarction; STEMI = ST elevation myocardial in farction.

Incomplete* = patients discontinued statin therapy single handed

Table 2. Demographics (control group)

Participant	Age(y)	Sex	Education	Type of MI	Statin	Daily Dosage(mg)	Side effects	Adherence	Months after MI
P013	61	F	Unknown	STEMI	Atorvastatin	40	None	Complete	1
P014	62	M	MSc	STEMI	Atorvastatin	40	None	Complete	1
P015	66	F	BSc	NSTEMI	Atorvastatin	80	Muscle Cramps	Complete	1
P016	64	M	Highschool	STEMI	Atorvastatin	80	None	Complete	6
P017	61	F	Unknown	STEMI	Atorvastatin	40	None	Complete	6
P018	69	F	MSc	STEMI	Atorvastatin	40	Muscle Cramps	Complete	6
P019	76	M	MSc	NSTEMI	Atorvastatin	40	None	Complete	12
P020	55	M	BSc	STEMI	Atorvastatin	40	None	Complete	12
P021	61	F	BSc	STEMI	Atorvastatin	40	None	Complete	12
P022	66	M	Unknown	STEMI	Atorvastatin	40	Muscle Cramps	Complete	12

BSc= bachelor of science; F= female; M= male; MG= milligram; MI = myocardial infarction; MSc = master of science;

NSTEMI = non ST elevation myocardial infarction;

VII

Test Results

Table 3 shows test results, ranked highest to lowest, with patients' ITQ and PQ scores for the intervention group. Median pre-test score was 13 out of 50 (IQR 17) points. The pre-test showed that 8 (67%) patients recalled that statins had *some* effect on cholesterol in the body, however 7 (60%) patients could not elaborate *what* the underlying mechanism was (i.e. lowering of cholesterol and reducing atherosclerosis, preventing new cardiovascular events). Median post-test score was 21 out of 50 (IQR 11) points; a median increase of 8 (IQR 8) points after three weeks (table 3). Test improvement was mainly related to an increase of understanding that statins have a lowering effect on cholesterol, positively affecting atherosclerosis in the coronary vessels and thereby preventing new cardiovascular events; 10/12 (83%) patients could explain that effect in their own words.

The control group scored a median post-test score of 6 out of 50 points (IQR 4)(table 4); the post-test showed that 8 (80%) patients recalled that statins had *some* effect on cholesterol in the body, however 8 (80%) patients could not elaborate *what* the underlying mechanism was (i.e. lowering of cholesterol and reducing atherosclerosis, preventing new cardiovascular events etc.).

Two patients had no knowledge of why they used statins. In comparison to the intervention group, the control group test score after conventional education (T=0, figure 1) was slightly lower (6 points vs 13 points, p=.02). Comparing all control-group and intervention-group patients at 1 month of follow up, median test scores were comparable (10 points vs 13 points, p=.4).

ITQ and PQ outcome

Table 3 shows ITQ and PQ outcomes. Median Immersive Tendency score was 63(IQR 26), median Presence score was 83(IQR 23). Highest ITQ scores were observed among 5 out of 6 (83%) best performing patients (highest test improvement).

Highest PQ scores were observed among 3 out of 6 (50%) best performing patients (highest test improvement). Immersive tendencies were moderately positive correlated with test improvement (r=0.56, p<.05), whereas presence was not correlated with test improvement (r= 0.038, p=.4).

Table 3. Test and questionnaire outcomes with ranks (intervention group).

Patient	Pre-test	Post-test	TI	Rank TI	ITQ	Rank ITQ	PQ	Rank PQ
P001	9	24	15	1	82	2	61	12
P003	12	26	14	2	67	6	88	4
P011	20	33	13	3.5	81	3	93	3
P012	7	20	13	3.5	84	1	80	8
P007	24	35	11	5	79	4	81	7
P009	17	26	9	6	52	10	86	5
P005	1	9	8	7.5	47	12	95	1
P004	15	23	8	7.5	56	8	70	11
P006	15	21	6	9	51	11	94	2
P008	9	12	3	10	74	5	77	9
P010	6	5	-1	11	54	9	84	6
P002	21	16	-5	12	59	7	72	10

ITQ = immersive tendencies questionnaire; PQ = presence questionnaire; TI = test improvement

VII

Table 4. Post-test outcome (control group).

Participant	Post-test score	Months after MI
P013	6	1
P014	10	1
P015	15	1
P016	6	6
P017	6	6
P018	5	6
P019	10	12
P020	6	12
P021	12	12
P022	1	12

MI = myocardial infarction

Qualitative Outcome - User Comments on the HoloLens Application.

Forty three comments were shared. Four themes were identified through content analysis: i) general usability of the HoloLens, ii) visibility and understanding of statin function, iii) visibility of coronary atherosclerosis and iv) usability of the app in the cardiology department. Table 3 gives an overview of example excerpts.

Regarding *general HoloLens use,* 3/12 (25%) patients noted that the healthcare professional should control the app and three other commented that the added value of an MR was minimal in comparison to a video.

Statin function was overall clear to 8/12 (75%) of patients. *Atherosclerosis* was visible however underexposed in the app according to 6/12 (50%) patients; "…the narrowing of the blood vessels is clear to me and the effect of statins on it…", "…*how* atherosclerosis develops is missing from the app…" and "…you can't see the process of calcification in the vessels…".

Regarding *overall use during hospital admission*, 6/12 (50%) of patients noted that the app should be shown to patients right after myocardial infarction in the hospital; "…if I had seen this earlier I would have understood more why I was hospitalized…", "…

I think I would have understood my heart attack better if this was shown to me…" and "…a few days after treatment it would be good to see what led to the heart attack and how it could be prevented…" were typical comments. Overall, none of the intervention group patients mentioned cyber-sickness related complaints during use of the MR-application (table 3).

Table 3. Example excerpts.

Visibility and understanding statin function	"… this helps me understand what happened and what statins do…" "… the statin function is clear to me now…" "…it reaches the goal of letting me understand my medication…"
Visibility of coronary atherosclerosis	"…the diminished blood flow and stenosis can be more dramatic; this looks too 'cute'/'childish'. "… I want to know more about how a stenosis develops…" "…a text in the app saying that blood flow is diminished might be useful…" "… the direct effect of statins on stenosis is clear and very useful…" "… If I had seen this right after my infarction, it would have made understanding it much easier…"
General use of the app in the hospital	"..this is very useful in the overall outpatient care process, maybe with my own data…' "…I am too old for this; not for my generation…" "…this technology needs some practice…"
Overall usability of HoloLens technology	"…this is amazing!..." "…the goggles are too heavy…" "…the doctor should guide the patient with the model…"
Cybersickness	No complaints regarding nausea, motion sickness or loss of vision or disturbed vision were mentioned by the intervention group.

VII

Discussion

Principal Findings

To summarize the findings of the current study, it primarily shows that after myocardial infarction, overall intervention and control group patients have limited understanding of statins. However, it shows that an MR model on statin function can be used in clinical practice: ten of twelve (83%) patients improved their statin knowledge after using the HoloLens application. Secondly, stated by patients, MR seems a feasible medium to extend the possibilities of visual education, especially during the clinical admission of myocardial infarction. This study provides insight in how a collaboration with patients leads to the development of optimized educational tools to implement in clinical practice after myocardial infarction.

Education on Statin Function and Health Behavior

Statin non-adherence is still a contemporary problem which is well illustrated in a recent randomized study by Wood et al, showing that, despite the small study sample, 50% of enrolled cardiovascular disease patients would not resume statin therapy because of experienced side effects(9).

Although patients primarily tend to discontinue statin therapy due to side effects, medical- or non- medical opinions and a lack of understanding the importance of the drug increase the problem further(33, 34). Healthcare professionals can improve statin adherence foremost by highlighting the importance of it.

The secondary preventive effect of statins after myocardial infarction is beyond dispute and stressed by all international guidelines (35, 36), still statin non-adherence is a common phenomenon in myocardial infarction patients(37, 38). A seventh of patients in our study discontinued statin therapy, which is comparable to scientific literature(38, 39).

In line with a previous study concerning patient education after myocardial infarction(25), our results identically shows that patients have minimal understanding of statins after myocardial infarction after conventional education, both in the interventional and control group. To overcome knowledge gaps, and become familiar with the disease and medication, patients rate visual aids of high importance in education after myocardial infarction(40).

The question remains if patient education improves statin adherence, as data in this matter is scarce and limited to smaller studies(11, 41). To improve statin adherence, patients' representation of the treatment should be met by the professional(42-44). When education is goal-oriented, for example promote statin adherence, adoption of new information into this behavior will be more effective. As stated by the cognitive load theory by Sweller(45), this theory states that education becomes effective when the methods of information exchange (i.e. presentation of information) promotes low extraneous cognitive load. Conventional methods (i.e. booklets) in the outpatient setting of myocardial infarction patients create high levels of cognitive load, whereas visual methods, such as videos or the MR model, create low levels of cognitive load(45). The use of MR has been proven useful in medical education for students (18, 21) and professionals(46, 47) and it might be a feasible medium for patients as well as our study suggests. To test if this promotes long-term statin adherence, requires further study.

Future Development of MR in the Clinical Domain

The double-diamond human centered design approach used in this study is becoming more frequent in medical research(28, 29, 48). This structured method promotes scientific reasoning during the process of scientific research. Although often described in literature as a concept, studies describing development and utilization of an end-product are scarce. Our study is the first to use the double diamond approach to assess a clinical problem in myocardial infarction patients and hint at a solution with an MR device.

The majority of patients (83%) in our study improved their knowledge on statins by using the developed MR application, despite low levels of involvement and focus for digital environments. This implies that the MR app might be effective in myocardial infarction patients, regardless if a patient has a high or low tendency to become focused and immersed in digital environments. Half of participants stated they would have wanted to use this technology during the initial admission of their myocardial infarction, to understand the disease mechanisms and the long term effects of medication better.

Both findings add to the existing body of evidence that visualization might be a feasible method to educate myocardial infarction patients. Both offer insight in further development of MR technology in the clinical domain after myocardial infarction, which, to our knowledge, is not discussed in the literature so far. To develop the application further and test its clinical effectiveness, the double diamond approach can be utilized further to specify additional features. Although the technology takes some time to get adjusted to, this can be overcome by letting the physician take the lead. An MR application on a HoloLens can be shared between multiple HoloLenses, enabling a visual interactive collaboration between physician and multiple patients thus enabling group education for instance during rehabilitation. Additionally, the coupling with a desktop-version of the app could support the usability in the outpatient setting. The strength of MR technology lies in the possibility to see both physician and educational model without closing of the real world (as with Virtual Reality), thus minimizing fear of claustrophobia or simulator sickness.

Although a basic heart model was used for our prototype, visual ultrasound and angiographic data can be incorporated in the moving model, making the visualizations patient specific.

The same model can then be used to show for instance changes in left ventricular function over time or new found anomalies in the coronary anatomy after angiography. As suggested, MR promotes interactivity, irrespective of the age of the patient. A study by Rohrbach et al showed in octogenarian Alzheimer patients that a HoloLens application effectively supported activities of daily living in these patients(17). Overall, further testing and comparing this technology to contemporary educational methods such as booklets and videos, is eminent.

Limitations

There are certain limitations to our study that need to be taken into account when interpreting the results. Firstly, the assessed study group is small and only consisted of myocardial infarction patients. Unfortunately, including more patients was restricted due to the COVD-19 pandemic of 2020 and 2021. A larger study population with patients of diverse cardiovascular diseases requiring statin use, could strengthen our results further. Secondly, the majority of patients included in our study were below 65 years. Although a feasible medium in older patients, this MR app should be tested in octogenarians as well.

Thirdly, no longitudinal test scores were gathered in both control and intervention group. Fourthly, clinical end-points, such as patients' LDL value during follow-up, were measured during this study. Lastly, further *randomized* studies between conventional and novel technologies are needed to assess the added value in patient education.

Conclusion

An MR statin education application can be applied effectively in myocardial infarction patients to explain statin function and importance. The use of a MS HoloLens is feasible for this purpose, with no effect of individual immersive tendencies on the educational process observed. The present study offers insight into the direction and development of modern visual educational tools in cardiology.

References

1. Kahn T. World Health Organization - Cardiovascular Diseases: World Health Organization; 2020 [Available from: https://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1.
2. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European heart journal. 2018;39(2):119-77.
3. Sivashanmugarajah A, Fulcher J, Sullivan D, Elam M, Jenkins A, Keech A. Suggested clinical approach for the diagnosis and management of 'statin intolerance' with an emphasis on muscle-related side-effects. Internal medicine journal. 2019;49(9):1081-91.
4. Saxon DR, Eckel RH. Statin Intolerance: A Literature Review and Management Strategies. Progress in cardiovascular diseases. 2016;59(2):153-64.
5. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Revista espanola de cardiologia (English ed). 2017;70(12):1082.
6. Abd TT, Jacobson TA. Statin-induced myopathy: a review and update. Expert opinion on drug safety. 2011;10(3):373-87.
7. Bellosta S, Corsini A. Statin drug interactions and related adverse reactions: an update. Expert opinion on drug safety. 2018;17(1):25-37.
8. Krüger K, Leppkes N, Gehrke-Beck S, Herrmann W, Algharably EA, Kreutz R, et al. Improving long-term adherence to statin therapy: a qualitative study of GPs' experiences in primary care. Br J Gen Pract. 2018;68(671):e401-e7.
9. Wood FA, Howard JP, Finegold JA, Nowbar AN, Thompson DM, Arnold AD, et al. N-of-1 Trial of a Statin, Placebo, or No Treatment to Assess Side Effects. The New England journal of medicine. 2020.
10. Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. Health technology assessment (Winchester, England). 1998;2(14):i-iv, 1-74.
11. Jones AS, Ellis CJ, Nash M, Stanfield B, Broadbent E. Using Animation to Improve Recovery from Acute Coronary Syndrome: A Randomized Trial. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2016;50(1):108-18.
12. Williams B, Anderson AS, Barton K, McGhee J. Can theory be embedded in visual interventions to promote self-management? A proposed model and worked example. International journal of nursing studies. 2012;49(12):1598-609.
13. Devcich DA, Ellis CJ, Broadbent E, Gamble G, Petrie KJ. The psychological impact of test results following diagnostic coronary CT angiography. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 2012;31(6):738-44.

14. Perera AI, Thomas MG, Moore JO, Faasse K, Petrie KJ. Effect of a smartphone application incorporating personalized health-related imagery on adherence to antiretroviral therapy: a randomized clinical trial. AIDS patient care and STDs. 2014;28(11):579-86.
15. Kaphingst KA, Persky S, McCall C, Lachance C, Loewenstein J, Beall AC, et al. Testing the effects of educational strategies on comprehension of a genomic concept using virtual reality technology. Patient education and counseling. 2009;77(2):224-30.
16. Becker A, Herzberg D, Marsden N, Thomanek S, Jung H, Leonhardt C. A new computer-based counselling system for the promotion of physical activity in patients with chronic diseases--results from a pilot study. Patient education and counseling. 2011;83(2):195-202.
17. Rohrbach N, Gulde P, Armstrong AR, Hartig L, Abdelrazeq A, Schroder S, et al. An augmented reality approach for ADL support in Alzheimer's disease: a crossover trial. Journal of neuroengineering and rehabilitation. 2019;16(1):66.
18. Bogomolova K, van der Ham IJM, Dankbaar MEW, van den Broek WW, Hovius SER, van der Hage JA, et al. The Effect of Stereoscopic Augmented Reality Visualization on Learning Anatomy and the Modifying Effect of Visual-Spatial Abilities: A Double-Center Randomized Controlled Trial. Anatomical sciences education. 2020;13(5):558-67.
19. Biglino G, Capelli C, Wray J, Schievano S, Leaver LK, Khambadkone S, et al. 3D-manufactured patient-specific models of congenital heart defects for communication in clinical practice: feasibility and acceptability. BMJ open. 2015;5(4):e007165.
20. Wang S, Parsons M, Stone-McLean J, Rogers P, Boyd S, Hoover K, et al. Augmented Reality as a Telemedicine Platform for Remote Procedural Training. Sensors (Basel, Switzerland). 2017;17(10).
21. Bogomolova K, Hierck BP, Looijen AEM, Pilon JNM, Putter H, Wainman B, et al. Stereoscopic three-dimensional visualisation technology in anatomy learning: A meta-analysis. Medical education. 2020.
22. Bray L, Sharpe A, Gichuru P, Fortune PM, Blake L, Appleton V. The Acceptability and Impact of the Xploro Digital Therapeutic Platform to Inform and Prepare Children for Planned Procedures in a Hospital: Before and After Evaluation Study. Journal of medical Internet research. 2020;22(8):e17367.
23. Tait AR, Connally L, Doshi A, Johnson A, Skrzpek A, Grimes M, et al. Development and evaluation of an augmented reality education program for pediatric research. Journal of clinical and translational research. 2020;5(3):96-101.
24. Sezer S, Piai V, Kessels RPC, Ter Laan M. Information Recall in Pre-Operative Consultation for Glioma Surgery Using Actual Size Three-Dimensional Models. Journal of clinical medicine. 2020;9(11).
25. Hilt AD, Mamaqi Kapllani K, Hierck BP, Kemp AC, Albayrak A, Melles M, et al. Perspectives of Patients and Professionals on Information and Education After Myocardial Infarction With Insight for Mixed Reality Implementation: Cross-Sectional Interview Study. JMIR human factors. 2020;7(2):e17147.

26. Witmer BJ, Singer MJ. Measuring Presence in Virtual Environments: A Presence Questionnaire. Presence. 1998;7(3):225-40.
27. Eleven lessons: managing design in eleven globar brands - A study of the design process. London, 2005: The Design Council; 2007.
28. Ferreira FK, Song EH, Gomes H, Garcia EB, Ferreira LM. New mindset in scientific method in the health field: Design Thinking. Clinics (Sao Paulo, Brazil). 2015;70(12):770-2.
29. Melles M, Albayrak A, Goossens R. Innovating Health Care: Key Characteristics of Human-Centered Design. International journal for quality in health care : journal of the International Society for Quality in Health Care. 2020.
30. Unity - Game engine, tools and multiplatform. 2020 [Available from: https://unity.com/products.
31. Weibel D, Schmutz J, Pahud O, Wissmath B. Measuring Spatial Presence: Introducing and Validating the Pictorial Presence SAM. 2015;24(1):44-61.
32. Wissmath B, Weibel D, Schmutz J, Mast FW. Being present in more than one place at a time? Patterns of mental self-localization. Consciousness and cognition. 2011;20(4):1808-15.
33. Mauskop A, Borden WB. Predictors of statin adherence. Curr Cardiol Rep. 2011;13(6):553-8.
34. Campione JR, Sleath B, Biddle AK, Weinberger M. The influence of physicians' guideline compliance on patients' statin adherence: a retrospective cohort study. Am J Geriatr Pharmacother. 2005;3(4):229-39.
35. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(7):2160-236.
36. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140(11):e596-e646.
37. Hickson RP, Robinson JG, Annis IE, Killeya-Jones LA, Fang G. It's Not Too Late to Improve Statin Adherence: Association Between Changes in Statin Adherence from Before to After Acute Myocardial Infarction and All-Cause Mortality. J Am Heart Assoc. 2019;8(7):e011378.
38. Colantonio LD, Rosenson RS, Deng L, Monda KL, Dai Y, Farkouh ME, et al. Adherence to Statin Therapy Among US Adults Between 2007 and 2014. Journal of the American Heart Association. 2019;8(1):e010376.
39. Eindhoven DC, Hilt AD, Zwaan TC, Schalij MJ, Borleffs CJW. Age and gender differences in medical adherence after myocardial infarction: Women do not receive optimal treatment - The Netherlands claims database. European journal of preventive cardiology. 2018;25(2):181-9.
40. Scott JT, Thompson DR. Assessing the information needs of post-myocardial infarction patients: a systematic review. Patient education and counseling. 2003;50(2):167-77.
41. Nieuwkerk PT, Nierman MC, Vissers MN, Locadia M, Greggers-Peusch P, Knape LP, et al. Intervention to improve adherence to lipid-lowering medication and lipid-levels in patients with an increased cardiovascular risk. The American journal of cardiology. 2012;110(5):666-72.

42. O'Donovan CE, Painter L, Lowe B, Robinson H, Broadbent E. The impact of illness perceptions and disease severity on quality of life in congenital heart disease. Cardiol Young. 2016;26(1):100-9.
43. Rajpura JR, Nayak R. Role of illness perceptions and medication beliefs on medication compliance of elderly hypertensive cohorts. J Pharm Pract. 2014;27(1):19-24.
44. Hagger MS, Hardcastle SJ, Hu M, Kwok S, Lin J, Nawawi HM, et al. Effects of medication, treatment, and behavioral beliefs on intentions to take medication in patients with familial hypercholesterolemia. Atherosclerosis. 2018;277:493-501.
45. Sweller J. Cognitive Load During Problem Solving: Effects on Learning. 1988;12(2):257-85.
46. Bogomolova K, van der Ham IJM, Dankbaar MEW, van den Broek WW, Hovius SER, van der Hage JA, et al. The effect of stereoscopic Augmented Reality visualization on learning anatomy and the modifying effect of visual-spatial abilities: a double-center randomized controlled trial. Anatomical sciences education. 2019.
47. Sauer IM, Queisner M, Tang P, Moosburner S, Hoepfner O, Horner R, et al. Mixed Reality in Visceral Surgery: Development of a Suitable Workflow and Evaluation of Intraoperative Use-cases. Annals of surgery. 2017;266(5):706-12.
48. Badwan B, Bothara R, Latijnhouwers M, Smithies A, Sandars J. The importance of design thinking in medical education. Medical teacher. 2018;40(4):425-6.
49. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. European heart journal. 2013;34(38):2949-3003.

VII