Chapter

Actual as well as Future Technologies and Noninvasive Devices for Optimal Management of Diabetes Mellitus and Chronic Heart Failure

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Abstract

In recent years, several technological innovations have become part of the daily lives of patients suffered from chronic diseases. It is the case for diabetes mellitus and chronic heart failure with noninvasive glucose sensors, intelligent insulin pumps, artificial pancreas, telemedicine, and artificial intelligence for an optimal management. A review of the literature dedicated to these technologies and devices supports the efficacy of the latter. Mainly, these technologies have shown a beneficial effect on diabetes or chronic heart failure management with mainly improvement for these two diseases of patient ownership of the disease; patient adherence to therapeutic and hygiene-dietary measures; the management of comorbidities (hypertension, weight, dyslipidemia); and at least, good patient receptivity and accountability. Especially, the emergence of these technologies in the daily lives of these patients suffered from chronic disease has led to an improvement of the quality of life for patients. Nevertheless, the magnitude of its effects remains to date debatable or to be consolidated, especially with the variation in patients' characteristics and methods of experimentation and in terms of medical and economic objectives.

Keywords: chronic disease, diabetes mellitus, chronic heart failure, noninvasive device, glucose sensors, intelligent insulin pumps, artificial pancreas, telemedicine, telemonitoring, artificial intelligence, Big Data

1. Introduction

According to the World Health Organization (WHO), "chronic disease" is defined as a long-term condition that changes over time, for example, high blood pressure, diabetes mellitus, chronic heart failure (CHF) or chronic obstructive

pulmonary disorders (COPD), cancer, chronic kidney diseases, cognitive impairment and deterioration, etc. [1, 2].

In France, it is estimated that 15 million people (about 20% of the population) are projected to suffer from chronic disease compared to 30% of the population in Canada and in other developed countries [2].

To date, despite major therapeutic advances, most chronic diseases remain serious in terms of functional or survival prognosis, with high morbidity and mortality rates [1]. Yet, this type of disease is responsible for 17 million deaths worldwide each year. A 5-year mortality rate of 30–50% has been reported in patients with New York Heart Association (NYHA) stages III–IV CHF [3]. In this setting, patients also frequently present for emergency hospitalization and rehospitalization, with long hospital stays, resulting in impaired quality of life [1, 3]. In France, acute and chronic HF is thus responsible for over 210,000 hospitalizations per year [1, 2], accounting for 5% of all hospitalizations and being the main cause of hospitalization among elderly subjects.

Optimal management of these chronic diseases is a challenge for health professionals. In recent years, progress has been made thanks to molecular biology with the development of innovative therapies, for example, new drugs, cellular therapy, etc. [3–5]. They also benefit from major advances in technologies (e.g., sensors, infusion systems, connected objects, etc.) and in artificial intelligence (AI) (e.g., Big Data analysis, deep learning, etc.) [6]. Combined with the information and communication technologies (ICT) and the social and educational sciences, these technological advances and derived tools will probably revolutionize the care of chronic diseases with an optimization of the management [7].

This chapter focuses on actual as well as future technologies and noninvasive devices used in clinical routine at the service of the patients with chronic disease, with the example of diabetes and CHF.

2. Noninvasive sensors for glucose equilibration

Several studies have demonstrated that the external rapid analogue infusion pump associated with the Flash Glucose Monitoring™ system (Abbott Laboratories) (**Figure 1**) is currently the reference management for patients undergoing intensive insulin therapy [9]. In particular, these studies have documented the benefits on HbA1c, the frequency of acute hypoglycemic and hyperglycemic episodes,

Figure 1.
Flash Glucose Monitoring™ system from Abbott Laboratories (adapted from [8]).

For the diabetic patient, self-monitoring with a capillary blood glucose meter has long been the only way to understand his or her blood glucose control [10]. This self-monitoring gives a more or less truncated reflection of glycemic control (subject to interpretation) and above all allows the patient to adapt his insulin administration. In this setting, Holter glycemia, followed by real-time continuous glucose measurement in the 2000s, revolutionized our vision of glycemic control [6, 10].

In recent years, noninvasive connected sensors measuring interstitial glucose continuously have become more accurate, gradually freeing themselves from calibration constraints (e.g., FreeStyle Libre™, Abbott Laboratories) or from drug interference (e.g., paracetamol), operating for longer and longer (15 days–6 months) and becoming more discreet by placing themselves under the skin (Eversense™, Senseonics/Roche Diabetes Care) [10, 11]. The improvement in their accuracy (meaning mean absolute relative difference [MARD], from 16–20% to 10–14%) allows direct adaptation of insulin without concomitant control of capillary blood glucose levels [11].

3. Noninvasive sensors for glucose self-management

Clinical studies have validated this method, which replaces the classic capillary self-monitoring of blood glucose in the management of patients treated with intensive insulin therapy. Controlled clinical studies have shown the efficacy of these devices on the improvement of HbA1c, associated with a decrease in the time spent in hypoglycemia, in T1D under external pump, but also under multi-injection (Dexcom STS™ System, Dexcom, Inc.) [11]. In addition, their efficacy has also been confirmed in T2D, in pregnant women and in children [12].

The connection of the sensors and the possible sharing of data (Dexcom G5™ Mobile, Dexcom, Inc.) allows a joint analysis of these data by the patient, the parents of a child, the doctor, or the nurse, thus avoiding, thanks to rapid adaptation of the treatment, deterioration in glycemic control. Interstitial glucose data, glycemic variability, and time spent in the target defined for a patient complete the old "hard" criteria of HbA1c and frequency of hypoglycemia.

In some industrialized countries (e.g., in France), the reimbursement by health insurance companies of these devices (e.g., FreeStyle™ Libre, Abbott laboratories) and the soon-to-be-announced reimbursement of sensors coupled to external pumps for highly unstable type 1 diabetic patients opens the way to another modality of the concept of glycemic control assessment [10].

4. Intelligent insulin pumps

For type 1 diabetic and numerous type 2 diabetic patients (e.g., with cardiovascular complications), insulin therapy is the necessary treatment. In this setting, fast or slow insulin analogues are usually administered subcutaneously, with one or more injections per day (e.g., multiple injections in intensive therapy) [4, 9]. In recent years, progress has been made with the development of ultrafast analogues (aspart Fiasp™, Novo Nordisk laboratory, recently launched on the French market), which allow the maximum peak action to be advanced and reduce the duration of action and therefore the quantity of insulin "on board," by about 10 minutes [4]. Nevertheless, the limitations of subcutaneous administration remain related to the still too long insulin kinetics, the reproducibility of imperfect absorption, and the absence of a first hepatic passage that is physiological.

In this context, studies have been carried out with the intraperitoneal route of administration. Compared to the subcutaneous route, this latter improves the HbA1c and is associated with a decrease in the frequency of severe hypoglycemia [13]. The outer surface of the peritoneum appears to be a promising site, and some bioartificial pancreases already use this route (e.g., BAir™, Beta-O2 Technologies and MailPan™ [for Macrocroencapsulation of Pancreatic ILôts], Defymed Company), with kinetic and metabolic results comparable to those of the intraperitoneal route [10]. An access port device allows for optimized insulin delivery either by an external pump or by injections. On this model, the device ExOlin™ (Defymed Company) is under development [14]. ExOlin™ is a medical device for the physiological delivery of insulin. ExOlin™ allows instantaneous intraperitoneal (IP) injection of insulin by simple subcutaneous injection (via an external connection to a syringe, pen, insulin pump, etc.). It includes a biocompatible, non-biodegradable membrane that is permeable to insulin but impermeable to the tissues of the recipient.

The connection of the Enlite™ sensor to the MiniMed Veo™ and 640G™ pumps (Medtronic Company) allows the automatic stopping of insulin infusion when a low interstitial glucose concentration is detected or predicted, dramatically reducing the occurrence of severe hypoglycemia (**Figure 2**) [9].

The recent reimbursement by the health insurance of this system in certain poorly balanced T1D patients, subject to severe hypoglycemia under insulin therapy by pump and adapted self-monitoring, allows for management within the framework of the care of this precursor of the "artificial pancreas."

Several "bolus calculators" have been developed, especially for the insulin pumps, offering a bolus dose by coupling the current blood glucose level and a predetermined insulin/glucose ratio [7]. Nowadays, these systems have been replaced by new intelligent systems based on algorithms (AI) [7, 12].

These latter make it possible to propose a real adaptation of prandial and basal doses by integrating several parameters (glycaemia, insulin sensitivity, etc.) specific to the patient phenotype (personalized medicine). Self-learning, they are specifically adapted to the patient's history of glycemic variations. They have shown their effectiveness on HbA1c, without increasing hypoglycemia, especially when coupled with nursing "coaching" (Diabeo™, Sanofi Laboratory) [16]. This system is currently approved within the framework of telemedicine [7]. Coupled with an external 670G™ pump (Medtronic Company), other algorithms already allow automatic adaptation of basal rates, with the patient managing only bolus doses [12].

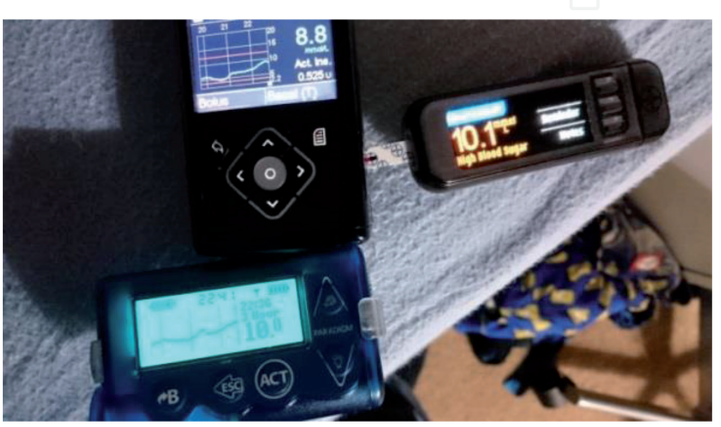

Figure 2.
Enlite™ sensor and MiniMed Veo™ 640G™ pumps from Medtronic Company (adapted from [15]).

5. Artificial pancreas for glycemic management

The artificial pancreas device system is a system of devices that closely mimics the glucose regulating function of a healthy pancreas [17]. Most artificial pancreas consists of three types of devices: a continuous glucose monitoring system (CGM); an insulin infusion pump; and a blood glucose device. A computer-controlled algorithm connects the CGM and insulin infusion pump to allow continuous communication between the two devices. An artificial pancreas device system not only monitors glucose levels in the body but also automatically adjusts the delivery of insulin to reduce high blood glucose levels (hyperglycemia) and minimize the incidence of low blood glucose (hypoglycemia) with little or no input from the patient "the diabetic patient's dream." Its efficacy had been proven in 2015 in one prospective study (ambulatory care of diabetic patients) and confirmed in a recent meta-analysis (24 studies including 585 patients) [17, 18]. This later had documented a significant improvement in the time spent in the target, the reduction of HbA1c and mean blood glucose, without an increase in hypoglycemia [18].

To date, the artificial pancreas is based on a closed-loop insulin delivery system, integrating AI. Most of these devices are mono-hormonal (insulin) and semiautomatic, with the patient manually reporting food intake and physical activity. Many of these devices are expected to be quickly brought to market (e.g., Diabeloop™ from Medtech Company) [19].

The limitations of single-hormonal subcutaneous devices are related to sensor latency, kinetics of interstitial glucose changes, and reproducibility of peripheral administration of subcutaneous insulin. In this setting, the bi-hormonal approach (insulin-glucagon) poses technical problems, as the stability of glucagon and the necessity of double reserves, but seems interesting to avoid hypoglycemia, especially during physical exercise [17, 18].

The addition of amylin or glucagon-like peptide-1 (GLP1) receptor analogue improves post-meal blood glucose levels by decreasing glucagon secretion; future years should make it possible to clarify the place of these molecules in the artificial pancreas.

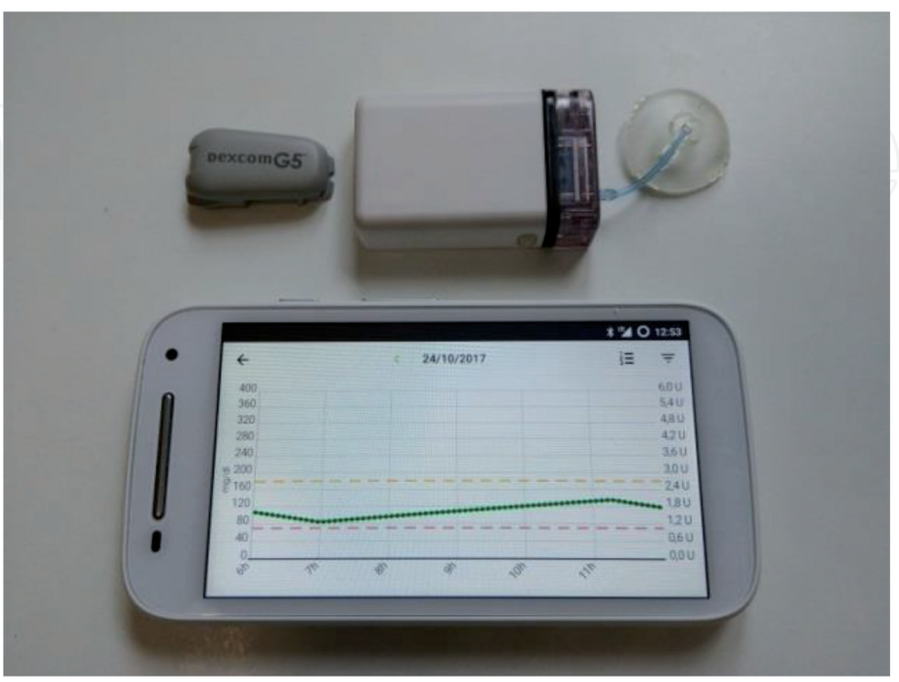

Figure 3.
Diabeloop™ from Medtech Company (adapted from [22]).

Another approach would be to operate other sites that combine sensors and insulin delivery. A study combining a subcutaneous sensor and intraperitoneal insulin infusion showed better regulation of post-meal periods [20]. Intraperitoneal insulin, which is more physiological, could improve problems related to meals and physical activity. Projects to miniaturize the implantable system and reduce its cost are all assets for make it an attractive alternative.

Improving the skills and the capacities of algorithms, by using the database setup (Big Data analysis), optimizing their self-learning capacity and their patient-specific adaptation capacity, and supplementing their information with multiple sensors collecting parameters other than blood glucose levels could allow early detection of food intake, physical activity, stress, and adaptation of the system to specific situations (children, pregnancies, highly unstable diabetes) [21]. The connection of the system to a telemedicine and coaching platform is an evolution that is already underway in the system Diabeloop™ (**Figure 3**).

6. Telemonitoring in the setting of diabetes and chronic heart failure

Over the last 10 years, new-generation telemedicine projects and studies have been developed in the setting of chronic disease management, particularly in the case of telemonitoring [7, 23]. Compared to the first projects, most of these projects incorporate self-administered medical questionnaires or forms on symptoms and signs of diabetes or chronic heart failure (CHF) decompensation; tools for medical education, particularly disease self-appropriation, food hygiene, and physical activity; tools for patient motivation; tools for therapeutic and hygiene observance; tool to remote comorbidities (e.g., arterial hypertension, obesity, dyslipidemia); tools for interaction between the patient and healthcare professionals like telephone support centers, tablets, and Web sites (e.g., Edu@com project for diabetes and e-care project for CHF) (respectively, **Figures 4** and **5**) [7, 23].

6.1 Telemonitoring in the setting of diabetes

In the setting of diabetes, the analysis of first-generation projects and studies shows that remote monitoring showed improvements in control of blood glucose

Figure 4.
Telemedicine project for diabetic patients: Educ@dom (adapted from [24]).

Figure 5.
Telemedicine project for patients with chronic heart failure: e-care (adapted from [12]).

level, significant reduction in HbA1c; better appropriation of the disease by patients; greater adherence to therapeutic and hygiene-dietary measures; positive impact on comorbidities (arterial hypertension, weight, dyslipidemia); better patient's quality of life; and at least, good receptiveness by patients and patient empowerment [7, 23]. Moreover, a cost-effectiveness analysis found a potential of medical economy.

However to date, the magnitude of its effects remains debatable, especially with the variation in patients' characteristics (e.g., background, ability for self-management, and medical condition), sample selection, and approach for treatment of control groups.

Over the last years, new-generation telemedicine projects and studies have emerged in the setting of T1D and T2D [23, 25–27]. They support transmission and remote interpretation of patients' data for follow-up and preventive interventions. **Table 1** lists the characteristics of the telemonitoring studies conducted in the field of diabetes during the period from 2010 to 2015 (**Table 1**) [23, 25–27]. These new-generation telemedicine projects are often known as "telemedicine 2.0" projects, given that they all utilize new ICT and the Web (tools for the "e-Health 2.0") [27].

These projects rely on the standard connected tools for monitoring diabetes, such as glucose meters, BP, heart rate monitors, weighing scales, and pulse oximeters, which relay the collected information via Bluetooth, 3G, or 4G [7, 28]. They include continuous glycemic monitoring solution and often a video call.

The development of practical chemical sensors to monitor parameters, although less mature, is also feasible. However, some external glucose pumps for the chronic management of diabetes also contain chronic intermediate-term (i.e., several days) subcutaneous glucose monitoring capability. The ability of such chemical sensors to augment other device monitoring capabilities for heart failure or other risks will require investigation.

Name of the study	Results
The Utah remote monitoring project (n = 109)	Principal criteria: • Mean HbA1c had decreased from 9.73% at baseline to 7.81% at the end of the program (p < 0.0001) • Systolic blood pressure (BP) had decreased from 130.7 mmHg at baseline to 122.9 mmHg at the end (p = 0.0001) Secondary criteria: • Low-density lipoprotein content had decreased from 103.9 mg/dL at baseline to 93.7 mg/dL at the end (p = 0.0263) • Knowledge of diabetes and arterial hypertension have increased significantly (p < 0.001 for both) • Patient engagement and medication adherence also have improved, but not significantly • Per questionnaires at study end, patients felt the telemonitoring program had been useful
Randomized trial on home telemonitoring for the management of metabolic and cardiovascular risk in patients with type 2 diabetes (n = 302)	Principal criteria: • Mean HbA1c difference of 0.33 ± 0.1 (p = 0.001) has been observed between the telemonitoring compared and the control group. The proportion of patients reaching the target of HbA1c (HbA1c <7.0%) had been higher in the telemonitoring group than in the control group after 6 months, 33.0 vs. 18.7% (p = 0.009), and 12 months, 28.1 vs. 18.5% (p = 0.07) • No difference had been registered for body weight, BP, and lipid profile Secondary criteria: • For quality of life (evaluated with the 36-item short-form health survey), significant differences in favor of the telemonitoring group, as for physical functioning (p = 0.01) and mental health (p = 0.005) • On an economic level, a lower number of specialist visits was reported in the telemedicine group: incidence rate ratio of 0.72 (95% confidence interval: 0.51–1.01; p = 0.06)
Study assessed the utility and cost-effectiveness of an automated diabetes remote monitoring and management system (DMRS) (n = 98)	Principal criteria: • No significant difference for mean HbA1c between the DRMS and control groups at 3 months, 7.60 vs. 8.10%, and at 6 months, 8.10 vs. 7.90% (p = ns) Secondary criteria: • Changes from baseline to 6 months have been not statistically significant for self-reported medication adherence • Changes of diabetes-specific quality of life have been not significantly registered, except for the daily quality of life-social/vocational concern subscale score (p = 0.04)

Name of the study	Results
Telescot diabetes pragmatic multicenter randomized controlled trial (n = 321)	Principal criteria: • The mean (SD) HbA1c at follow-up was 7.92% in the intervention group vs. 8.36% in the usual care group. For primary analysis, adjusted mean HbA1c was 0.51% lower (95% CI: 0.22–0.81% (principal criterion) (p = 0·0007)) Secondary criteria: • Adjusted mean ambulatory systolic BP has been 3.06 mmHg lower (95% CI: 0.56–5.56 mmHg, p = 0.017), and mean ambulatory diastolic BP has been 2.17 mmHg lower (95% CI: 0.62–3.72, p = 0.006) among people in the intervention group when compared with usual care after adjustment • No significant differences were identified between groups in terms of weight, treatment pattern, and adherence to medication or quality of life • The number of telephone calls was greater between nurses and patients in the intervention compared with control group, rate ratio of 7.50 (95% CI: 4.45–12.65, p < 0.0001), but no other significant differences between groups in use of health services were identified between groups

Table 1.
Results of the telemonitoring studies conducted in the field of diabetes during the period from 2010 to 2015 [23, 25–27].

6.2 Telemonitoring in the setting of chronic heart failure

Over the last 10 years, several new-generation telemedicine projects and trials have emerged in the era of CHF, particularly in Europe [29]. These projects have main objectives: the prevention and treatment of HF exacerbations and the promotion of self-empowerment. Main projects are listed in **Table 2**.

Most of these projects rely on the usual connected tools for monitoring HF, such as blood pressure meters, heart rate monitor, weighing scales, and pulse oximeters, which relay the information collected via Bluetooth, 3G, or 4G [7, 29]. They also incorporate self-administered medical questionnaires or forms (symptoms and signs of HF); tools for medical education, particularly disease self-appropriation, food hygiene, and physical activity; tools for patient motivation; tools for therapeutic and hygiene observance; and tools for interaction between the patient and healthcare professionals like telephone support centers, tablets, and Web sites [29].

Telemonitoring can also be divided in passive or automated, typical of implantable invasive devices that send either sporadically or continuously data to the receiving physician, and active, where, on the contrary, noninvasive devices involve an action or a self-measurement (e.g., blood pressure measurement) that a patient needs to accomplish. While the role of implantable telemonitoring devices for multiparameters or cardiac hemodynamic activity monitoring has been recently established as an effective way to prevent frequent hospitalizations, the role of noninvasive methods for the remote monitoring of CHF patients is still under debate. In this review, we will concentrate, in specific, on the role of external devices and of the electrocardiography for the remote monitoring of CHF patients.

Name of the study	Results
The Trans-European Network—home-care management system (n = 426)	Compared to standard care alone, mortality and rehospitalization rates were shown lower in the groups receiving either telemonitoring or nurse telephone support, without any statistically significant differences between both intervention groups
The BEAT-HF study (n = 437)	All-cause readmissions within 180 days post-discharge occurred in 50.8% (363 of 715) patients from the intervention group versus 49.2% (355 of 722) of those from the control group (adjusted hazard ratio, 1.03 [95% CI: 0.88–1.20]; p = 0.74)
The TIM-HF (n = 710)	All-cause mortality rate (primary end point) was 8.4 per 100 patient-years of follow-up in the telemedicine group and 8.7 per 100 patient-years of follow-up in the standard care group, without significant difference (OR: 0.97 [95% CI: 0.67–1.41]; p = 0.87)
The Telemedical Interventional Management in Heart Failure II (TIM-HF2) (n = 1570)	The percentage of days lost due to unplanned cardiovascular hospital admissions and all-cause death was 4.88% (95% CI: 4.55–5.23) in the remote patient management group versus 6.64% (6.19–7.13) in the standard care group (ratio 0.80, 95% CI: 0.65–1; p = 0.0460)

Table 2.
Results of the telemonitoring studies conducted in the field of chronic heart failure during the period from 2005 to 2018 [7, 29].

In the context of CHF, the number and variety of physiologic sensors and the useful clinical parameters derived from those sensors is likely to continue to increase rapidly [29]. For example, in addition to the capabilities described above, future devices may include additional sensors to track respiration parameters (including rate, minute ventilation, and perhaps apnea and dyspnea detection), tissue perfusion (via optical sensors), cardiac output and stroke volume (via impedance acute ischemia or myocardial infarction via S-T segment monitoring), electrical alternant, and heart rate turbulence. Indeed some recently released devices already contain some of these fascinating capabilities. To date, several projects include BNP monitoring, ECG monitoring, and even a video call [6, 29, 30].

Recently, the TIM-HF2 study is the first to well document the interest of telemedicine in the CHF field, resulting in clinically relevant outcomes with statistical significance (**Table 2**) [31]. In fact, the percentage of days lost due to unplanned cardiovascular hospital admissions and all-cause death was 4.88% (95% CI: 4.55–5.23) in the remote patient management group versus 6.64% (6.19–7.13) in the standard care group (ratio 0.80, 95% CI: 0.65–1; p = 0.0460). Patients assigned to remote patient management lost a mean of 17.8 days (95% CI: 16.6–19.1) per year compared with 24.2 days (95% CI: 22.6–26) per year for patients assigned to standard care. The all-cause death rate was 7.86 (95% CI: 6.14–10.10) per 100 person-years of follow-up in the remote patient management group versus 11.34 (95% CI: 9.21–13.95) per 100 person-years of follow-up in the standard care group (hazard ratio [HR] 0.70, 95% CI: 0.5–0.96; p = 0.0280) (**Figure 6**) [31].

Cardiovascular mortality did not significantly differ between both groups (HR 0.671, 95% CI: 0.45–1.01; p = 0.056).

For this TIM-HF2 care strategy, the key component was a well-structured telemedical center with physicians and HF nurses ("coordination center") available 24 hours a day and every day a week, able to act promptly according to the individual patient risk profile [7, 31]. The actions taken by the telemedical center staff included changes in medication and admission to hospital, as needed, in addition to educational activities.

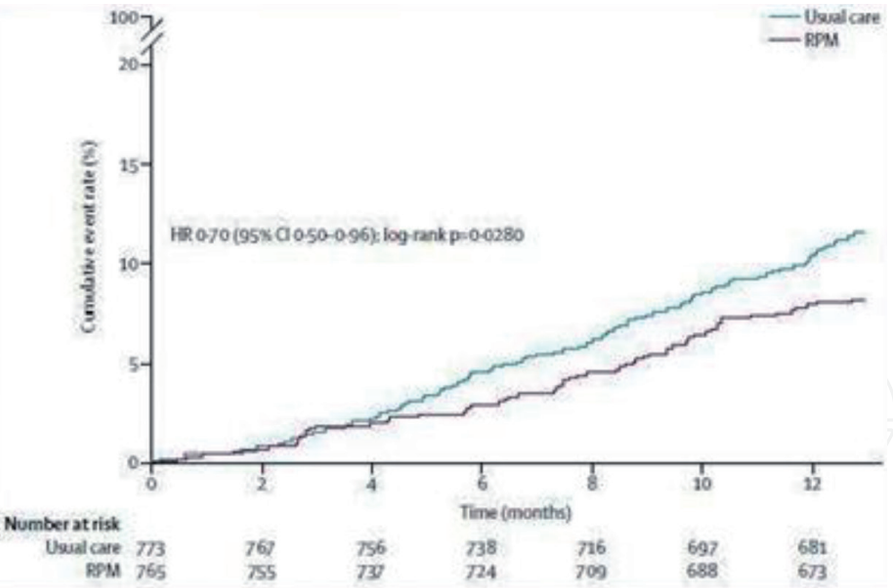

Figure 6.
TIM-HF2 trial (n = 1515). Rate of cumulative events in patients randomly assigned to remote patient management (n = 796) or usual care (n = 775) (adapted from [31]).

7. Artificial intelligence for diabetes and chronic heart failure management

In recent years, several informatic solutions or tools have been developed and used to optimize the management of chronic diseases as diabetes or CHF, for example, artificial neural network (ANN) algorithms, data mining software, and ontology [6, 7]. In this context, three clinical datasets are of particular interest: patients' phenotype; patients' electronic medical records containing physicians' notes, laboratory test results, and other information on diseases, treatments, and epidemiology that may be of interest for association studies and predictive modeling on prognosis and drug responses; and literature knowledge including rules and/or diabetes or CHF management [7, 32].

7.1 Artificial intelligence in telemonitoring in the setting of diabetes

In the setting of diabetes, two telemedicine projects use AI in order to be able, firstly, to adjust the blood glucose level to the patient's activity (software Diabeo™, Sanofi Laboratory) [16] and, secondly, to predict patient risks of diabetes decompensation [33]. In this later situation, the cloud-based software aggregates, cleans, and analyzes patient data to allow for identifying patterns that may indicate potential risks and provide predictive insights on healthcare outcomes, as the software MyPredi™ (Predimed Technology Company) [7, 33].

In the TeleSage study, T1D patients were randomized to usual quarterly follow-up (G1), home use of a smartphone recommending insulin doses (Diabeo™ software) with quarterly visits (G2), or use of the smartphone with short teleconsultations every 2 weeks but no visit until point end (G3) [12, 21]. At 6-month, the mean HbA1c level is 8.41 ± 1.04% in G3 versus 8.63 ± 1.07% in G2 versus 9.10 ± 1.16% in G1 (p = 0.0019 for G1–G3 comparison) (**Figure 7**) [16, 26]. The Diabeo™ system gave a 0.91% (0.60–1.21) improvement in HbA1c over controls and a 0.67% (0.35–0.99) reduction when used without teleconsultation. There was no difference in the frequency of hypoglycemic episodes or in medical time spent for hospital or telephone consultations. However, patients in G1 and G2 spent nearly 5 hours more than G3 patients attending hospital visits.

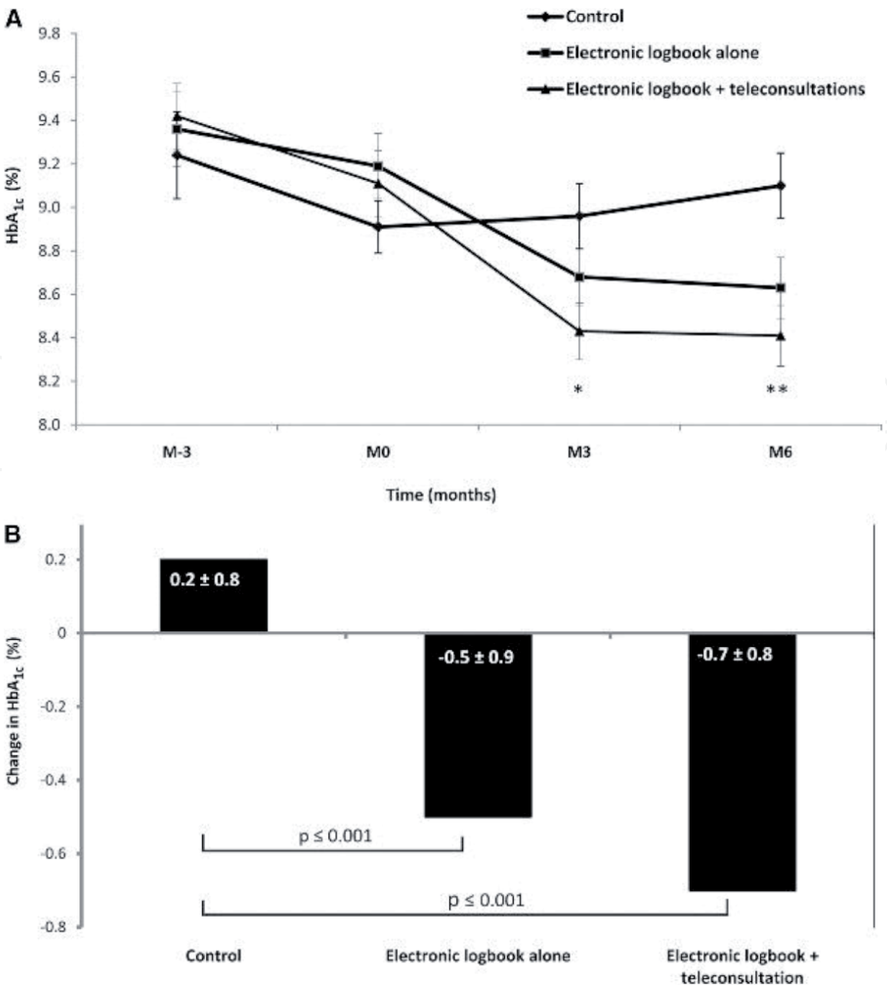

Figure 7.
*Efficacy of the software Diabeo™, licensed by Sanofi Laboratory (adapted from [21]). (A) HbA1c values (means ± SE), from 3 months before baseline to month 6. * p = 0.0103, ** p = 0.0019 compared with control group. (B) Change in HbA1c values (means ± SE) from baseline to month 6.*

The DIABETe telemonitoring project has been developed and designed to optimize home monitoring of diabetic patients by detecting, via a telemonitoring 2.0 platform, situations with a risk of decompensation of diabetes and its complications (e.g., myocardial infarction or CHF), the latter ultimately leading to hospitalization [33]. The AI of the DIABETe platform (MyPredi™) automatically generates indicators of chronic disease deterioration, that is, "warning alerts" for any chronic disease worsening, particularly diabetes, its macrovascular complications, and cardiovascular comorbidities (e.g., arterial hypertension and CHF). For the patient, these situations may lead to hospitalization if not treated appropriately. To our knowledge, this is one of the first projects that use AI in addition to ICT. The platform comprises connected nonintrusive medical sensors, a touchscreen tablet connected by Wi-Fi, and a router or 3G/4G, rendering it possible to interact with the patient and provide education on treatment, diet, and lifestyle (**Figure 8**) [7, 33].

The telemonitoring platform used in DIABETe was first validated in a monocentric study conducted in the Strasbourg University Hospital, carried out as part of the e-care project, primarily focused on the problem of CHF [34].

7.2 Artificial intelligence in telemonitoring in the setting of chronic heart failure

e-Care has been initially developed and designed to optimize home monitoring of CHF patients by detecting, via a telemonitoring 2.0 platform, situations with a risk of cardiac decompensation and rehospitalization. Between February 2014

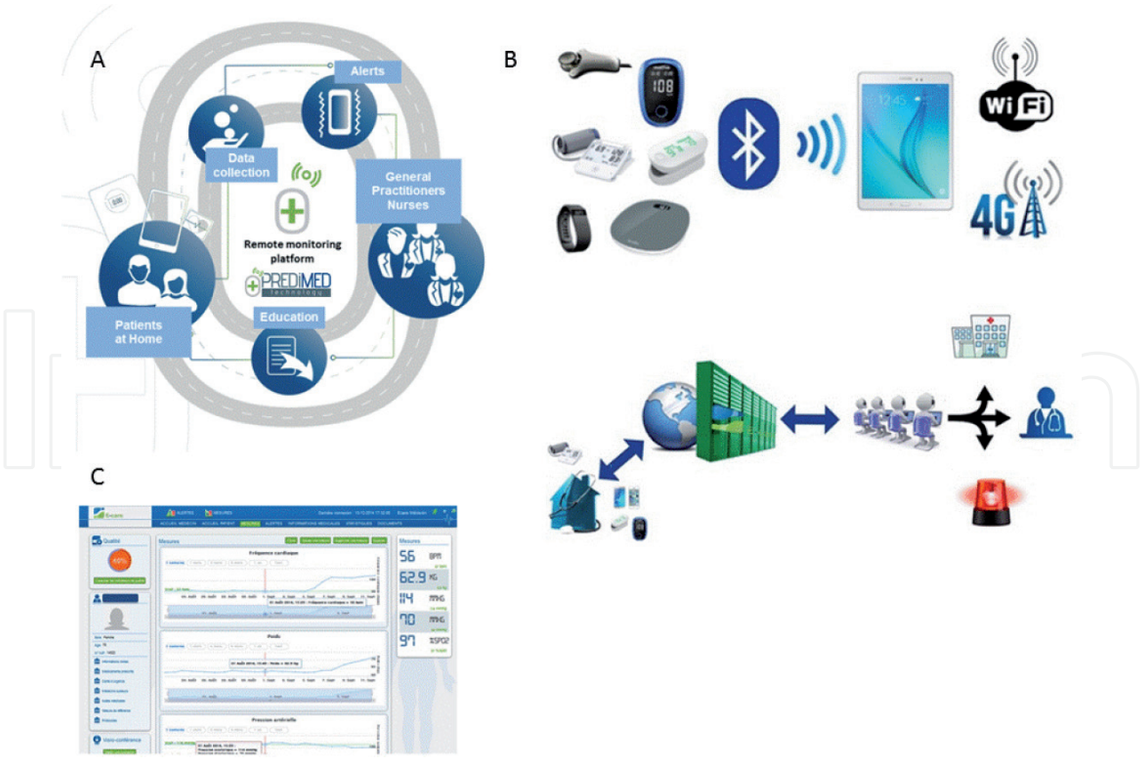

Figure 8.
Intelligent telemonitoring project on diabetes and/or chronic heart failure management. (A) The system is based on an inference engine and a medical ontology for personalized synchronous or asynchronous analysis of data specific to each patient and, if necessary, the sending of an artificial intelligence-generated alert (MyPredi™). (B) The platform comprises connected nonintrusive medical sensors, a touchscreen tablet connected by Wi-Fi, and a router or 3G/4G, rendering it possible to interact with the patient and provide education on treatment, diet, and lifestyle. (C) The system involves a server that hosts the patient's data and a secure Internet portal to which the patient and hospital- and non-hospital-based healthcare professionals can connect.

and April 2015, 175 patients were included into the e-care project [35]. During this period, the e-care platform was used on a daily basis by patients and healthcare professionals, according to a defined protocol of use specific to each patient. The mean age of these patients was 72 years, and the ratio of men to women is 0.7. The patients suffered from multiple concomitant diseases, with a mean Charlson index of 4.1. The five main diseases were CHF in more than 60% of subjects, anemia in more than 40%, atrial fibrillation in 30%, T2D in 30%, and chronic obstructive pulmonary disease in 30%. During the study, 1500 measurements were taken in these 175 patients, which resulted in the e-care system generating 700 alerts in 68 patients [35]. Some 107 subjects (61.1%) had no alerts upon follow-up. Follow-up data analysis of these 107 patients revealed that they exhibited no clinically significant events that might eventually have led to hospitalization. Analysis of the warning alerts showed that the e-care platform automatically and nonintrusively detected any worsening of the patient's health, particularly HF decompensation (between 2 and 9 days), with a sensitivity, specificity, and positive and negative predictive values of 100, 72, 90, and 100%, respectively. Both the healthcare professionals and patients, even the frailest, used the e-care system without difficulty until the end of the study. For nonautonomous patients, the system was employed by a nurse in addition to her other assigned tasks, such as washing and administering medication, or by close ones and family members [35].

To date, an enhanced version of the e-care platform and the AI (MyPredi™) will be experimented in the homes of CHF patients as part of a project called PRADO INCADO [7]. PRADO is a French program to support patients returning home after hospital, while PRADO INCADO will specifically target HF patients in this setting. Over a period of several months, it will follow 300 patients with NYHA Stages I–IV

HF using the PRADO organizational model for CHF patients developed by the national health insurance.

8. Conclusions

This review supports the efficacy of numerous current and new technologies and noninvasive tools for a better management of patients with chronic diseases, particularly diabetic patients and patients with CHF. Nevertheless, in chronic diseases, the magnitude of its effects remains to date debatable or to be consolidated, especially with the variation in patients' characteristics and methods of experimentation and in terms of medical and economic objectives.

To our opinion, innovative technologies based on AI (machine learning, Big Data) are going to build the future of chronic disease, and they invent the medicine of tomorrow.

Competing interest

M. Hajjam is the scientific director of Predimed Technology (www.predimed-technology.fr). All other authors have declared that no competing interests exist.

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