Automatic Dialysis and Continuous Renal Replacement Therapy: Keeping the Primacy of Human Consciousness and Fighting the Dark Side of Technology

Zaccaria Ricci^a Stefano Romagnoli^b Claudio Ronco^{c, d}

^aDepartment of Cardiology and Cardiac Surgery, Pediatric Cardiac Intensive Care Unit, Bambino Gesù Children's Hospital, IRCCS, Piazza Sant'Onofrio, Rome, ^bDepartment of Anesthesiology and Intensive Care, Azienda Ospedaliero-Universitaria Careggi, Largo Brambilla, Florence, ^cDepartment of Nephrology, Dialysis and Transplantation, San Bortolo Hospital, and ^dInternational Renal Research Institute of Vicenza (IRRIV), Vicenza, Italy

Acute and chronic dialysis therapies have evolved from a primordial and artisanal stage into a high-tech procedure with dedicated biomaterials and new devices [1]. A great part of the scientific evolution is concerned with the specific information and communication technology applied to dialysis machines [2]. The rapid changes in the patient during treatment and the inter-individual variability of clinical requirements have spurred new interest in the application of precision medicine to this area [3]. In particular, after an initial development of manual, semi-automatic, or fully automatic biofeedback control in chronic hemodialysis (HD), this approach is now turning into reality in the area of critical care nephrology and acute dialysis in the context of continuous renal replacement therapy (CRRT) [4, 5]. The complexity of the critically ill patients with acute kidney injury and other comorbidities requires a rapidly changing prescription modality followed by an immediate feedback from

the machine. Signals from the patient, laboratory medicine, and the extracorporeal circuit are integrated in a multi-input/multi-output expert system that makes immediate and accurate changes in treatment delivery by the machine. The feedback can be either authorized by the operator or directly executed by the machine without human intervention. The machine can automatically modify treatment time, dialysate composition, rates of filtration, and other parameters in order to achieve the desired therapeutic targets planned by the treating physician and set in the original prescription [6]. We are definitely far from the original scenario where physicians and nurses had to struggle with rudimentary machines in order to deliver a safe and effective treatment. Those times are gone, but with them, a great deal of knowledge of the internal mechanisms of acute and chronic dialysis has been lost. Often the dialysis/CRRT machine is seen as a black box where nothing can be modified from the sched-

uled functionality and the machine is automatically selecting the best operational mode to achieve therapeutic targets. Is this a positive progress or does this carry some drawbacks? Are we ready to enter the era of “automatic” HD and CRRT?

New discoveries and technical evolution have always not only attracted but also terrified human beings. Narrative literature is full of examples of this subconscious fear as in the case of the disquieting android of Philip Dick’s *Blade Runner*, the mental control operated by the matrix, or the apocalyptic view of destruction of earth by the Terminators. Although Isaac Asimov has clearly stated the behavioral rules for robots in the 3 Laws of Robotics, Hal 9000 of *2001: A Space Odyssey* and the WOPR supercomputer of *WarGames* presented a disturbed “personality” and did not operate within the law of safety for men. Since the original thinking of George Orwell, the collective imagination entails a pessimistic view about the incredibly rapid development of new sciences. Many questions are still without a clear answer. Will actually robots/devices be able to replace humans in most jobs? How soon will this happen? What are the human duties that machines will never be able to replace? Will artificial intelligence completely replace human cognitive functions? Is artificial intelligence an existential threat to humanity? Finally, can machines overpower humans? We have been asking ourselves whether these questions apply to HD and CRRT.

Indubitably, the benefits provided by current and emerging technologies, especially in medicine and research, are countless. We can monitor patient heart function by remote control. We can provide artificial prosthetics connected to central nervous system. Robotic-assisted surgery has become daily practice. We can analyze fetal genetic pattern in maternal blood. We can download a PDF article on our smartphone while attending a congress meeting and we can access the world literature at a glance. This is just to cite some of the simplest examples. The first of our ancestral fears probably relate to the loss of power and control. As automatic functions and reactions to specific events are left to computers and machines, human beings and physicians will become unprepared for unexpected emergencies, and they might regress to the point of becoming slaves of technology.

Airplanes have automations programmed into them that make it possible for an aircraft to land in dangerous weather conditions. New cars are programmed with autonomous driving and parking capabilities. In this view, artificial intelligence, mimicking “cognitive” functions, such as “learning,” “problem solving,” and “understand-

ing human speech,” induce both charm and fear at the same time.

The world of photography represents another example. We are routinely taking pictures of everyday life with any digital device available. Nowadays, photographs are cheap (if not free), easy, immediately shared, useful, and enjoyable. Still photography amateurs consider this “evolution” as a loss of technical capacity and identify this democratic moment of photographic explosion as the failure of such a noble art. Above all, modern cameras know how to fix exposure, enhance colors, and efficiently control highlights and, even in the “AUTO” mode, they simply work. If anything goes wrong, the subsequent Photoshop activity can fix the problem. But are these the photos that should represent the best moment in life? Should this standard become the rule for everybody? In the best-case scenario, the art of photography will be retained by a group of elite amateurs and professionals but the majority of people will have no clue of what is the focal and what is the diaphragm. We may wonder if the small elite point of view is justified. We may argue that the overwhelmingly high amount of “nice” photographs with respect to the past (when there was no warranty of results until the film was developed) is a positive consequence of this process. No more overexposed or dark portraits of the honeymoon. Is this an acceptable trade on the negative aspect that nobody knows anymore the fundamental rules of photography (framing, manual exposure, depth of field, quality of lenses, sensors’ dimensions, etc.)? Is an average (almost) acceptable quality of photographs a good thing or is it a betrayal of the photographer’s research for the Saint Grail (the perfect shot)? Is the possibility of photographing everything, everywhere, always, a real gain of our society, or is it the abdication of any critical selection for a “really meaningful” shot? (Not to mention the privacy issues).

So, if there is an entire world where machines can help humans and computers can solve difficult problems, where is the limit? Where should humans stop the transfer of functions and regain control of the system? These questions lead to the second of our ancestral fears: the possibility that the human tendency to make mistakes can transfer some wrong automations to automatic systems.

Moving with these doubts to the bedside, nowadays, average clinical activity and standards of care are certainly improved by protocolled medical decisions, especially when junior doctors are in charge and when the “average” patient is requiring a “regular” intervention. Improvement of sepsis management and outcome and the application of acute kidney injury preventive bundles are evi-

dent examples of guidelines' benefit [7]. On the other hand, physicians often dislike bundles, guidelines, and institutional recommendation due to the perception of constriction. Guideline-driven reactions are supposed as a complete loss of creativity, personal initiative, and direct role in patient care. The growing awareness of the importance of precision and personalized medicine is further contributing to a worsening of feelings toward guidelines, standardization, and recommendations [8]. Furthermore, these recommendations are often weak or not graded as best practice statements, and they should not represent a substitute for individual medical decision and single patient-oriented care. The apparent conflict between bundles/guidelines and personalized/precision medicine emerges clearly although the two approaches may also be seen as subsequent or parallel steps in the process of improving patient's care.

Technological development and automation have become crucial in all fields of medicine, including renal replacement therapy. Let us make the case, in the near future, of a CRRT machine capable (via complex algorithms and closed loops) to "automatically decide" how to optimize dose prescription in order to reach a preselected dialytic target. A young fellow is called at night to the intensive care unit (ICU) to evaluate the possible initiation of CRRT in an anuric, hemodynamically unstable, critically ill patient with hepatic failure. He plans to start CRRT immediately and, according to KDIGO guidelines [9], he prescribes a dose of 25 mL/kg/h of effluent flow for the first 24 h with heparin anticoagulation. Since he knows that the machine "thinks", he asks to connect the catheter to the system and then he leaves the ICU. The machine starts and progressively increases blood flow rate (Q_b). Since the catheter is not working properly, the "AUTO-mode system" will set Q_b at 100 mL/min in order to keep access pressure within preselected limits. The machine is now going to deliver 1,625 mL/h of effluent in a 65 kg patient (25 mL/kg/h according to the prescription) and eventually opts for continuous hemodiafiltration (CVVHDF) in post-dilution, with a filtration fraction not exceeding 20%. According to its algorithms, the machine splits the treatment into 1,000 mL/h of reinfusion and 625 mL/h of dialysate flow. After few hours of treatment, the transmembrane pressure starts rising and, after reaching the level of 250 mmHg, the machine switches the treatment to a full continuous dialytic modality (CVVHD), stabilizing transmembrane pressure and allowing the session to go on. The morning after, another colleague is having a coffee at the computer desk and, while holographically checking the CRRT treatment performance in the ICU (far from his computer room), real-

izes that the target dose is fully achieved and the treatment is continuing safely.

The prescribed treatment is achieved in a "common" patient requiring CRRT by an average physician (or pool of physicians) utilizing a fully automatic biofeedback technology. This case considers an advanced level of automatization in CRRT that, although not possible today, will probably represent the routine in the next generation's critical care ward. If we evaluate in detail the sequence of events, however, several problems are hidden below the superficial cover of an "adequate" correctly running CRRT. KDIGO recommendations represent (in 2017) a reference guide to start CRRT with a prescription of 20–25 mL/kg/h effluent flow. No evidence, so far, has established a correlation between CRRT modality (dialysis vs. hemofiltration) and outcome [10]. In our scenario, the machine initially followed the concept that the highest quote of convection should be delivered when possible. Subsequently, with the logical priority of saving circuit patency, the software automatically put such a first priority issue in a secondary place. Engineers must have performed a tough risk analysis and a thorough discussion to design this algorithm as acceptable. However, even if the above-described CRRT session is not really "harmful", we may consider it as far from "optimal" and potentially "inadequate". The machine is allowed to passively tackle the issue of vascular access malfunction. This aspect was not identified at the beginning of the session, the prescribing physician did not consider it and the nurses passively accepted it. It was superficially reviewed by others, and finally approved by a new apparently unaware operator of the morning shift. Furthermore, the software algorithms overrode the potential necessity for maintaining a convective component of the treatment, while the clinician did not acknowledge the problem thereafter.

It is indeed valuable to have tools helping inexpert operators or young fellows to act in the attempt of reducing potential harms and critical errors related to complex treatments. However, active critical reasoning should always be recommended and expected (human consciousness) in the rising "AUTO-mode era of CRRT." The safety of our patients may strongly depend on this attitude. The standard of care provided by automatic treatment delivery should not prevent further improvements provided by the "human factor."

Under the view of senior critical care nephrology "amateurs," it is our convinced opinion that personalization of treatments on patients' dynamic conditions should always be provided and automatic behaviors, even if harmless, should be constantly monitored, supervised, and reviewed.

Senior physicians should not slow down development and application of new technologies, but rather contribute to align knowledge with the novel achievements, keeping their fellows trained on all basic elements. In other words, we are recommending two steps in the process of an automated biofeedback procedure: the first is a careful analysis of the variables that play a role in the machine's decision and second is the full and responsible authorization of the changes proposed by the machine. The risk (or the dark side of this technology) is a completely passive acceptance of machine goal-directed therapy with no critical approach to the surrounding environment. Even worse, it may occur that a remote monitoring is made without direct contact with the patient. Medical science can fail if an algorithm instead of a bedside physician becomes the interface between technology and the patient.

Let's hypothesize that the circuit of the above patient, treated with the "automatic" CVVHD, would present a tiny rupture in the return line: the machine would register a decrease in outflow line pressure, interpreting it as the possibility of increasing blood flow due to improved catheter function. If such event occurred without any human intervention nor graphic warning, the patient could inadvertently suffer a dramatic blood loss before anyone would realize such issue. A smart and well trained nurse, instead, in the above case, would run to the bedside, taking control of the machine, stopping the treatment, and reducing the blood flow to a minimum (10 mL/min) in order to understand the origin of blood spillover and to eventually verify the possibility of quickly fixing the leak. In case he/she was successful, after sharing such option with the on-call physician, he could even consider the possibility to return, at least partially, the patient's blood before changing the circuit. On January 15, 2009, after a bird strike, US Airways Flight 1,549 successfully ditched in the Hudson River off midtown Manhattan [11]. It is unlikely to base such difficult decisions on automatic algorithms. This emergency procedure would not have been possible without fully trained and expert aviators. In fact, a question remains open concerning consciousness and the capacity of a machine to have a "free" decisional process, especially when this might lead to unexpectedly wrong decisions.

Probably it is not the loss of control that should scare humans (and physicians in particular), but the resignation to be fully instructed, adequately informed, timely updated. Modern mechanical ventilators automatically switch their ventilation mode from totally controlled, optimal in sedated patients without muscular activity, to totally assisted one, automatically proceeding with the weaning protocol. Nevertheless, if the patient stops

breathing, the safety system automatically intervenes by switching back the modality to a controlled one avoiding the risk of hypoventilation. This is the perfect example of a closed system that might induce us to fully trust the machine. Still, awareness of the ongoing process (in this case, patient weaning from ventilation), monitoring, supervision, and full knowledge of these "automata" is the only way to control the world surrounding us, whose continuous development cannot and should not be stopped.

The last concern regarding new technologies is about ethical aspects. In a not-so-far clinical scenario, physicians might ask/let machines to solve complex clinical cases. It may happen that the decisions necessary to keep this "automatic care" running will be so complex that human beings will be unable to cope adequately with them. At that point, we might have inadvertently delegated the full control of care to machines without the possibility to turn them off because of our high dependency. "All men by nature desire to know," said Aristotle, but the failure to understand the consequences of new knowledge is a common fault of physicians and scientists. They are often too taken by the quest of new discoveries to anticipate that newer and more powerful technologies can take on a life of their own. The new Pandora's box of automation in dialysis and CRRT has been opened and ideas cannot return to the box. The fear is that, by pursuing these technologies, we could create new threats to our patients in parallel with the evident benefits. Among the threats, there is the supine adaptation to a new dialysis therapy where the machine is a black box and no clear understanding of the process is retained nor requested. In such conditions, the cultural level of the treating physician will dramatically decrease due to loss of basic knowledge, control of the process, and ultimately human consciousness.

It is our role, as mentors, to prevent the dark side of technology from taking over the future generations.

References

- 1 Ronco C, La Manna G: Expanded hemodialysis: a new therapy for a new class of membranes. *Contrib Nephrol* 2017;190:124–133.
- 2 Ronco C: Evolution of technology for continuous renal replacement therapy: forty years of improvements. *Contrib Nephrol* 2017;189:114–123.
- 3 Cerdá J, Baldwin I, Honore PM, Villa G, Kellum JA, Ronco C; ADQI Consensus Group: Role of technology for the management of AKI in critically ill patients: from adoptive technology to precision continuous renal replacement therapy. *Blood Purif* 2016;42:248–265.

- 4 Schlöpfer P, Durovray JD, Plouhinec V, Chiappa C, Bellomo R, Schneider A: A first evaluation of OMNIh, a new device for continuous renal replacement therapy. *Blood Purif* 2016; 43:11–17.
- 5 Clark WR, Neri M, Garzotto F, Ricci Z, Goldstein SL, Ding X, Xu J, Ronco C: The future of critical care: renal support in 2027. *Crit Care* 2017;21:92.
- 6 Bagshaw SM, Chakravarthi MR, Ricci Z, Tolwani A, Neri M, De Rosa S, Kellum JA, Ronco C; ADQI Consensus Group: Precision continuous renal replacement therapy and solute control. *Blood Purif* 2016;42:238–247.
- 7 Levy MM, Rhodes A, Phillips GS, Townsend SR, Schorr CA, Beale R, Osborn T, Lemeshow S, Chiche JD, Artigas A, Dellinger RP: Surviving sepsis campaign: association between performance metrics and outcomes in a 7.5-year study. *Crit Care Med* 2015;43:3–12.
- 8 Wong HR: Intensive care medicine in 2050: precision medicine. *Intensive Care Med* 2017, Epub ahead of print.
- 9 Kidney Disease Improving Global Outcomes: KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2012;2:1–138.
- 10 Wald R, Friedrich JO, Bagshaw SM, Burns KE, Garg AX, Hladunewich MA, House AA, Lapinsky S, Klein D, Pannu NI, Pope K, Richardson RM, Thorpe K, Adhikari NK: Optimal mode of clearance in critically ill patients with acute kidney injury (OMAKI) – a pilot randomized controlled trial of hemofiltration versus hemodialysis: a Canadian critical care trials group project. *Crit Care* 2012;16:R205.
- 11 https://en.wikipedia.org/wiki/US_Airways_Flight_1549.