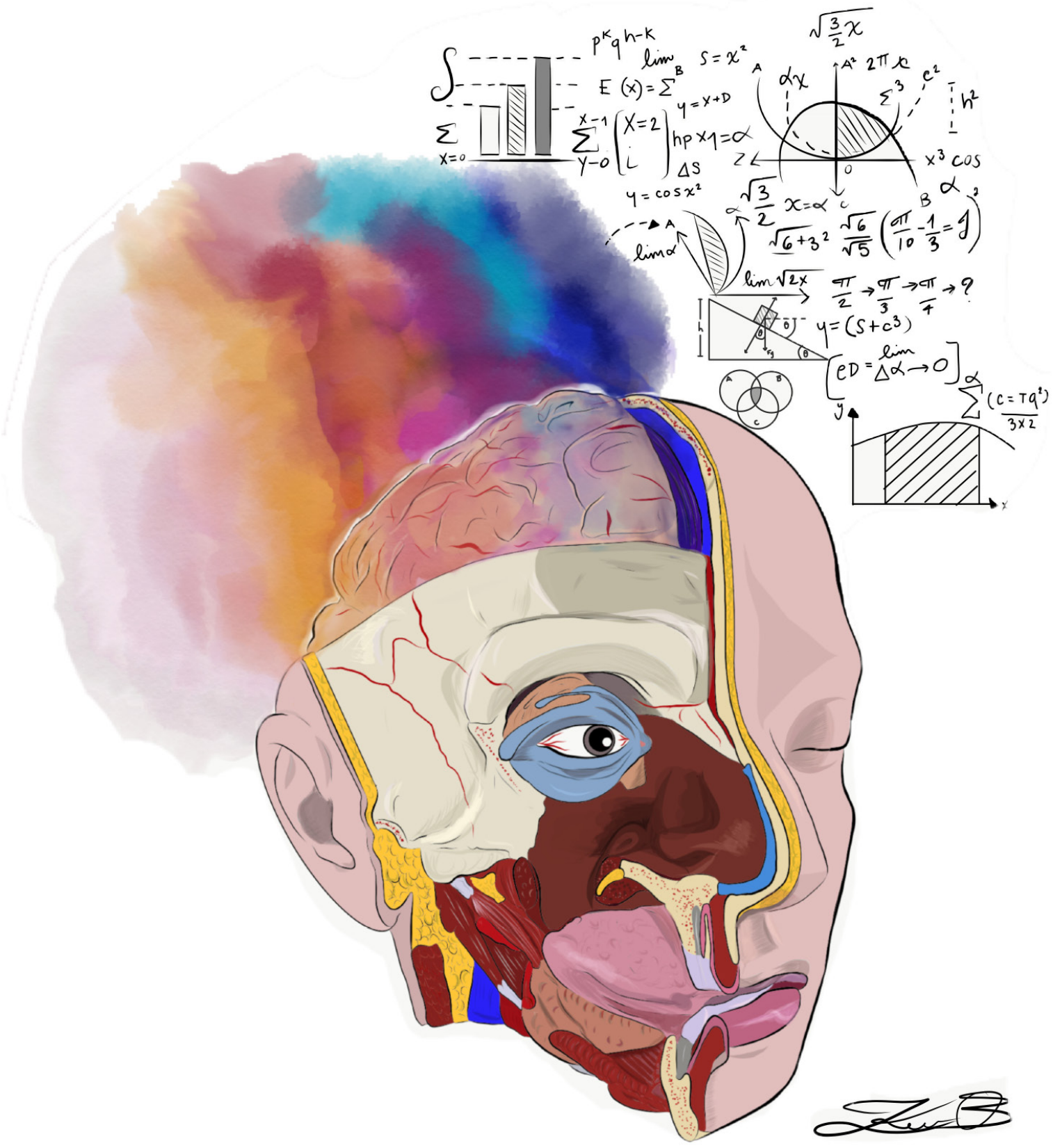
SACKLER JOURNAL OF MEDICINE

Volume 5 Issue 1



MISSION STATEMENT

What's emerging in medicine today? The Sackler Journal of Medicine – a forum where trends in medicine including translational research, the economics and policy of healthcare, and clinical experiences are explored, analyzed and discussed. SJM is a peer-reviewed journal for medical students to discuss and learn about the latest medical breakthroughs and the fundamentals of medicine.

We encourage student and physician collaboration to bring you literature reviews, case reports, original research, reflective pieces, and short commentaries on published papers. Take the opportunity to contribute your work, experiences and voice to the conversation.

SUBMISSIONS INFORMATION

Submissions from students, faculty, and individuals are welcomed. For more information please visit the "Submissions" page on the Sackler Journal of Medicine website at sacklerjom.org

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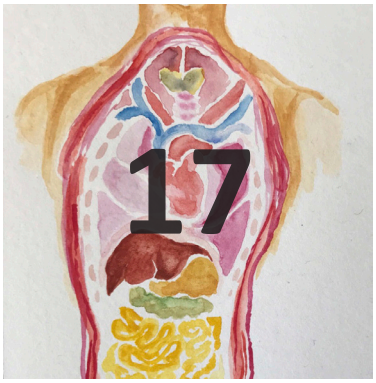
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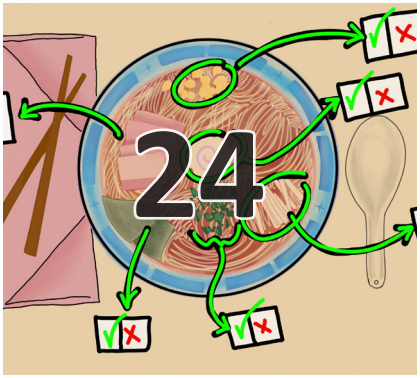
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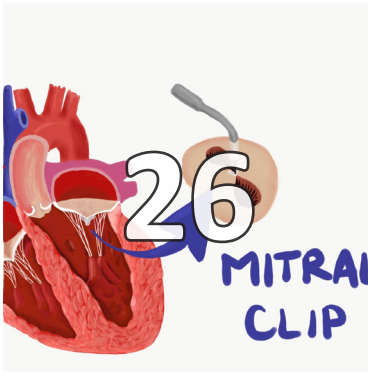
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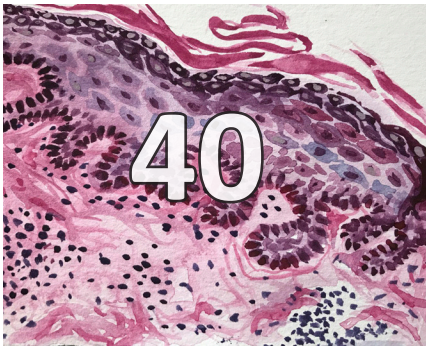
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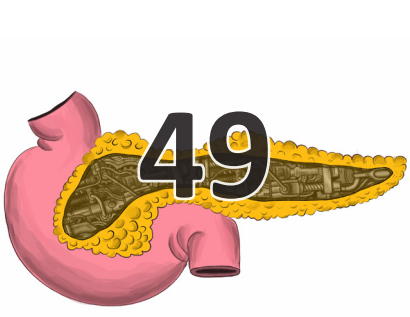
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Letter From the Editors

Micah Iticovici and Melissa Bendayan
Editors-In-Chief

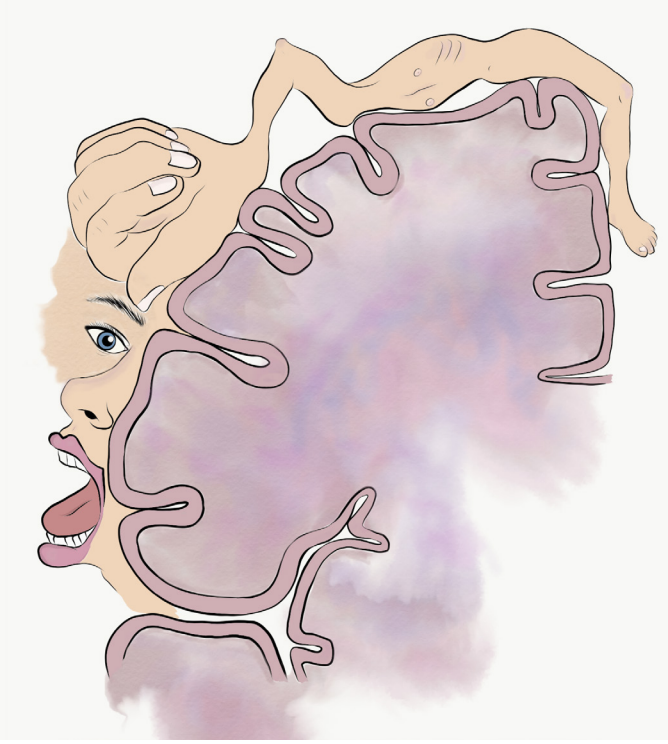
If you are reading this, we would like to congratulate you on the behalf of all of us at the Sackler Journal of Medicine, for two reasons. First, you have survived the COVID19 pandemic, and second, you are holding (or have downloaded the PDF version of) the first ever bi-annual edition of the Sackler Journal of Medicine. Due to unfortunate circumstances, the release of this issue was delayed, however, we are proud to publish an issue that is up to the same high standard as our usual annual publication. We are excited to have been part of the team that initiated the biannual issue of the Journal , and we look forward to seeing this continue in the future. We want to thank the team of editors, peer reviewers, and executive board for their tireless work, especially for their continued effort despite the challenges of the pandemic.

Putting aside massive global events, this has been an eventful year for the Sackler School of Medicine. As such, we at the Sackler Journal of Medicine would like to extend a warm greeting to Dr. Berger, the new Director of Pre-clinical studies. We wish him the best of luck. We would also like to address our fellow students regarding student life in the present day. Aside from its devastating effect on the global scale, COVID-19 has created a number of unprecedented issues for medical students worldwide, in addition to the many challenges we already face. Despite these issues facing us, it has shown how strong the ties between our classmates can be, and how much we can rely on each other for support. We can be proud of our Sackler community alongside our academic and scholastic successes in these times. With that, we would like to say goodbye, and look forward to see SJM continue to grow in the future.

We hope you enjoy the issue.

Sincerely,

Micah Iticovici and Melissa Bendayan
Editors-in-Chief



Artist: *Olivia Keller-Baruch*

Letter From Dr. Allen

Aaron Allen M.D.
Faculty Advisor- SJM
Deputy Director
New York State Program
Sackler Faculty of Medicine
Tel Aviv University
Israel

" When the world is turned upside-down"

Fellow members of the Sackler Family,

No one could have predicted that the spring semester of 2020 would essentially be swallowed up by the largest pandemic in the last 100 years. The events of the past few months will change and shape everything that comes after it for decades. People of all ages have learned to lead their lives with masks in public and with strict adherence to stay-home orders. Distance learning has taken over as a method not only to replace learning of basic science but even in place of clinical curriculum. We as members of the medical community are used to changes but at the same time so much of our normal has changed that we have begun to question our own desires and motivations for things that just a short time ago we took for granted.

Yet, as this terrible tragedy continues to upend hospitals, families, business and yes even medical schools I am reminded of a poignant story from World War II. A child in the Warsaw Ghetto asked his father on the night of Passover, "Father, as we sit together tonight I ask a new type of question to you- will we be together next year and will I get to sit with you at the Passover table next year as I sit with you this year?" The father wisely and knowingly answered. "Moshe my son, I don't know, but I do know that somewhere there will be another Moshe who will sit with his father at the Passover table and ask him questions like you are asking me tonight." So to it is with the profession of medicine. Many of colleagues both doctors and nurses and other health care workers have paid the highest price during these days trying to take care and keep their patients alive and well. So we ask, "What will happen to us? What will be with our school and our research in the coming year?"

The only answer is that each of us working together must realize that we must continue to learn and research and explore even in the darkest of times regardless of the personal losses both real and academic that we each suffer. It is in that vein, that I applaud the editors and writers of the Sackler Journal of Medicine for pushing forward and publishing this issue during the shadow of this terrible virus.

This is the light of medicine and research that can never be extinguished.

Aaron Allen M.D.

1st Place Award: The Villain

Meir Chodakiewitz
Sackler School of Medicine, Tel Aviv University, Tel Aviv

the villain

by meir chodakiewitz

they call me a villain, but I have a name.
as infinite cycles of time can attest,
I have been downtrodden.
suppressed, feared, hated,
excised, destroyed.
besieged by my own blood.
destitute, a bane, bemarked by shame.
they call me a villain, but I have a name.

born as one, and grown to two, anew,
only providence could have seen this through.
as doom looms near, I am to blame
yet our ancestors once chanted the same.
your creed, your will, I will not obey,
as time will supply my infinite reign,
I, we, the eternal, forever sustained.
they call us the villain, but we have a name.

metastasis.

Improving Operating Room Turnover in Robotic Surgery: A Human Factors Approach

Tara N. Cohen [a], PhD; Sarah E. Francis [b], MA; Maureen Fimpler [b], RN; Yosef Nasseri[b] MD;Jennifer T. Anger[b], MD, MPH, FACS; Kate A. Cohen[a], BA; Kevin Shamash[b] BS; Bruce L.Gewertz[b], MD, FACS; Raymund Avenido[b], MSN, RN; Daniel Shouhed[b],MD, FACS.

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Abstract

Background: Turnover time (TOT) has remained the subject of numerous scientific publications and operating room (OR) committee discussions. Inefficiencies associated with TOT are multiplied when complex technology, such as surgical robots, are involved. Using a human factors approach, this study investigated impediments to efficient robotic TOT and team members' perceptions surrounding this topic.

Study Design: Researchers observed 20 robotic turnovers over two months at a tertiary hospital. TOT, cleaning time, number of staff present, bed set-up time, instrument set-up time, and any major delays were recorded. Additionally, 79 OR team members completed a questionnaire regarding perceptions of OR turnover.

Results: Average TOT was 72 min (*s,* 24 min). Overall, cleaning required the most time (average of 27 min, 37.96% of TOT), followed by instrument set-up (15.5 min, 21.34% of TOT) and RN retrieval of the patient from pre-op (12 min, 17.72% of TOT). OR team members estimated on the questionnaire that turnovers require 60.36 min. Surgeons, anesthesiologists and residents believed that the greatest contributor to TOT was "time to set up the OR," while nurses and surgical techs rated "instrument availability" as the greatest issue.

Conclusions: *In situ* human factors observation of OR turnovers revealed several areas of opportunity for process improvement. Interestingly, OR team members' perceptions of TOT and contributing factors were different from the observed contributors. Three areas were highlighted for improvement: (1) cleaning time, (2) patient retrieval from pre-op, and (3) team member readiness for patient arrival. This data can be used to guide the implementation of targeted interventions to improve TOT efficiency.

Introduction

Turnover time (TOT), or the time required to clean and prepare an operating room (OR) between two surgical cases, has been the subject of numerous scientific investigations and OR committee discussions for several years. TOT is a common performance metric utilized to study OR efficiency because it represents necessary but non-income generating time in a sophisticated environment with highly trained staff, leading to high fixed costs (1,2).

Some have argued that aiming to reduce OR TOT is only beneficial when several operations of short duration are anticipated (3). However, even when reduced TOTs do not lead to an increased number of surgical cases in a given day, delays in care delivery contribute to dissatisfaction among patients and healthcare workers (4). This dissatisfaction is compounded by misconceptions about the root causes of OR delays among surgeons, anesthesiologists, and OR staff. Such misconceptions are due in part to confusion over OR scheduling, and also result from poor role and team definitions during turnover (1,5).

Therefore, achieving consistent, efficient TOTs requires OR staff to have well-defined roles, and clear task allocation and sequencing (5). Interventional studies have identified a lack of team cohesiveness among OR staff during turnover as a major barrier to efficiency (6). Without transparency and organization, confusion mounts as staff members across different

Artist: *Niko Morozov*

teams, including registered nurses (RNs), log techs, scrub techs (STs), environmental services (EVS), and anesthesia, are expected to conduct multiple concurrent tasks across different rooms.

A typical turnover begins as soon as the patient from the previous case is wheeled out of the OR. First, EVS staff members arrive to clean the room. Simultaneously, RNs chart specific actions and associated time points during the case, including when patients are wheeled into and out of the OR. However, RNs must be prepared to spring into action, given that task demands during turnover are high and require movement. RNs have been found to have as many as 10 different turnover-related functions across 7 different locations, with no standardized protocol for carrying out each function (7). Surgeons and residents perform non-operative work during turnover, while anesthesiologists travel to the PACU with the first patient and confirm the next case (6). Anesthesiologists then go to the pre-operative area, where they begin administering drugs to the patient in the next case, and then either wheel the patient into the OR, or remain in the OR to set up while the RN wheels the patient back (8). Scrub tech (ST) duties during turnover include case cart management, cleaning, and setting up the back table (5).

Previous studies have outlined various effective turnover interventions. The creation of dedicated teams staffed with STs and RNs familiar with specific procedures, performed by specific surgeons, has been found to increase efficiency and decrease distraction (9). To improve coordination among teams, some hospitals now deliver electronic cues to all OR staff members, creating a high standard of accountability (1). However, such technologies are not uniformly implemented, despite the fact that surgeons have reported that electronically-delivered alerts enhance their efficiency (10). Simple analysis of interactions between anesthesiologists, STs, and RNs has been found to be a minimal-cost method of improving turnover and surgical caseload during times when the OR is maximally staffed. The same study found that merely making nursing and tech aware of the aim to speed-up turnover can effectively reduce TOT (7).

As technology advances and surgical techniques adapt, procedures have become more complicated and involve new equipment, resulting in longer TOTs. For example, the use of surgical robots can multiply the inefficiencies associated with general surgery turnover. Introduction of this technology into the OR leads to more complex requirements including more surgical instruments, better communication between team members, and coordinating more elements (5). Unsurprisingly, studies have found that OR TOT for cases involving robotic surgery may be longer and more variable than those that do not utilize this technology (5-7).

The goal of this study was to investigate current barriers to efficient TOT in procedures involving surgical robots and to develop data-driven interventions aimed at improving workflow and more clearly defining team roles. This study considered interventions and turnover benchmarks that have proven useful in the past, and also sought to explore how attitudes and opinions can idiosyncratically shape TOT data and beliefs about time delay at different institutions.

Methods

Data Collection

Observations. Trained pre-medical students observed a sample of 20 robotic OR turnovers at a 900-bed tertiary care medical center over the course of two months. Each observer received three hours of training by a human factors expert (TC) and process improvement expert (SF). Specifically, training was broken down into the following segments: hour 1 – overview of the project, description of human factors, discussion of relevant terminology, personnel, equipment and common process and demonstration of the data collection tool; hour 2 – practice observation of a turnover and use of the tool; hour 3 – debriefing session to discuss missed items or questions. Four pre-med students underwent training, and only one observer was present during each turnover. Hospital

staff were aware of the presence and research goals of the observers. The hospital's research oversight committee approved the study and deemed it a quality-improvement project that did not involve human subjects.

Prospective data were collected for any turnover in which the previous case or the to-follow case utilized a robot for the procedure. Observers were present in the ORs from the time the patient of the previous case was wheeled out of the operating room until the patient of the to-follow case was wheeled into the operating room. Observers recorded total TOT, cleaning time, number of EVS team members present, bed set-up time, instrument set-up time and major delays associated with the turnover.

Surveys. Team member perceptions of operating room turnover were also investigated through the use of a survey developed in-house. The survey consisted of demographic questions including: (1) participant title; (2) participant specialty; (3) years in specialty; (4) years at the institution; (5) involvement with robotic surgery cases; and an additional set of questions aimed at investigating perceptions of operating room turnover: (1) satisfaction of efficiency of turnover (2) what aspects of turnover make an individual unsatisfied (3) factors that contribute to lengthy turnover (4) what a reasonable amount of time for turnover is (5) how long operating room turnover actually takes (6) any additional ideas to improve on turnover.

All operating room surgeons, nurses, residents, scrub techs and anesthesiologists were invited to take the survey. However, only the results from those who indicated participation in the robotic surgery cases were included in the results. All eligible participants were sent an email containing an information sheet about the study and a link to the online survey.

Results

Observations. Twenty robotic-related turnovers were observed in order to identify a baseline of process measures and times required to complete each task. Overall, TOTs averaged 72 minutes (s = 24 min). Cleaning the OR required the most time (average of 27 min, 37.96% of TOT), followed by instrument set-up (15.5 min, 21.34% of TOT), and RN retrieval of the patient from pre-op (12 min, 17.72% of TOT) (see Figure 1).

Survey. In total, 79 OR staff members completed the survey and indicated that they were involved with robotic surgery (Surgeons: 14; Anesthesiologists: 21; Nurses: 26; Surgical Techs: 8; Resident Surgeons: 10). Participants had on average 13.19 years of experience (s = 11.64) in their individual specialties and an average of 11.91 years (s = 11.15) of experience in their role at the institution.

When asked to rate their satisfaction with the current efficiency of TOT, the average score across all participants was 1.97 (on a scale of 1 – strongly dissatisfied to 5 – strongly satisfied). While there were no significant differences between the groups, surgeons were the most dissatisfied on average (score of 1.79), followed by residents (1.80) and anesthesiologists (1.81). Surgical techs and nurses were the least dissatisfied (2.13 and 2.35 respectively) (see Figure 2).

When asked to rank the factors that contribute most to TOT, answers differed significantly by group: Surgeons, Anesthesiologists, and Residents ranked

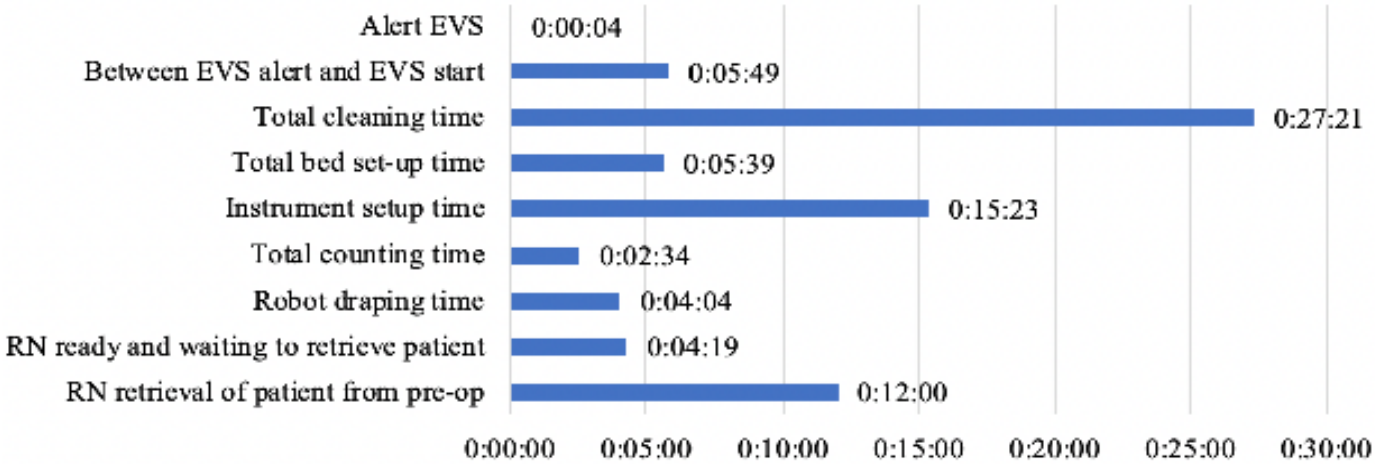

Figure 1: Average Time to Complete Tasks (hh:mm:ss)

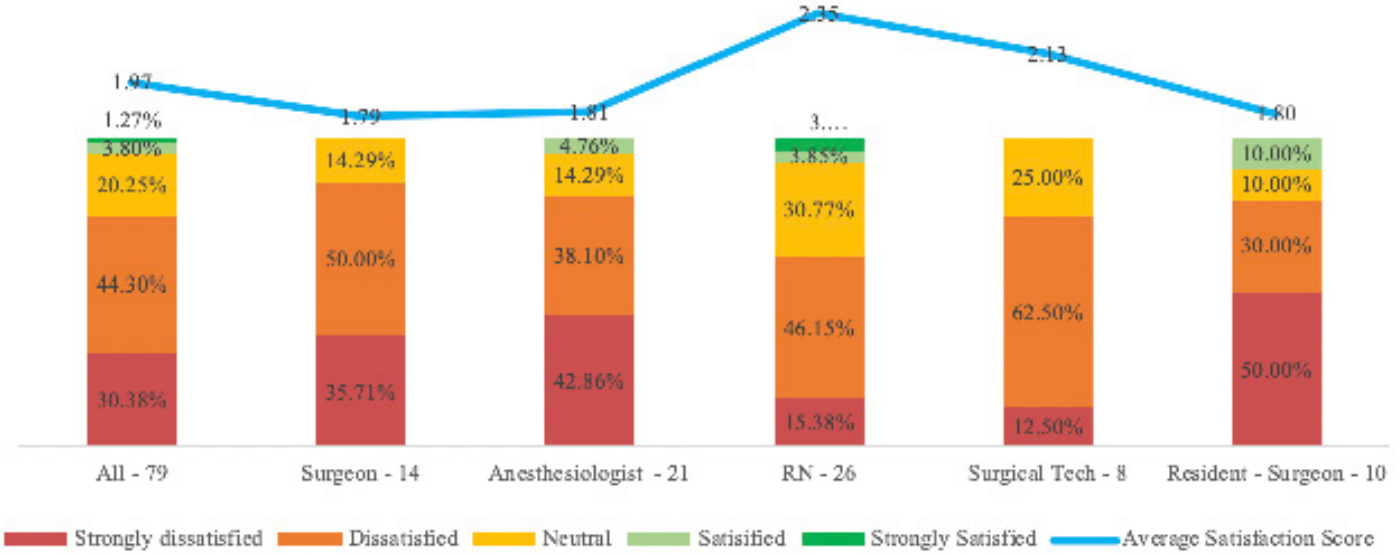

Figure 2: Satisfaction with efficiency of OR turnover

"time to set up the OR" as the greatest contributor, while STs and RNs assigned "instrument availability" as the greatest contributor (see Figure 3). Significant differences were found between three of the factors rated as contributors to TOT. A Kruskal-Wallis H test was run to determine if there were differences in contribution score of each of the variables between each of the 5 participant groups. Distributions of scores were not similar for all groups, as assessed by visual inspection of a boxplot. The mean ranks of EVS scores ($\chi^2(5) = 14.761, p = .011$), instrument availability scores ($\chi^2(5) = 33.930$, $p = .000$) and anesthesia readiness scores ($\chi^2(5) = 25.473$, $p = .000$) were statistically significantly different between groups of participants. In other words, the participants' role on the surgical team significantly affected how they ranked 3 factors that contribute to TOT; EVS, instrument availability, and anesthesia readiness.

Participants were asked to estimate the time associated with turnover and to provide a proposed "reasonable" amount of time for turnover. On average, all participants estimated that turnover required 59.48 min. ($s = 15.46$ min.). However, the estimated TOT was statistically significantly different for different groups ($F(4, 70) = 3.951$ $p < .006$). Specifically, surgeons estimated turnover required the most amount of time (71.93 min.), followed by residents (62.20 min.), anesthesiologists (57.57 min.), STs (56.86 min.) and RNs (53.26 min.). Overall, participants proposed an average TOT of 32.95 min. ($s = 10.19$) for the ideal time.

Discussion

The current study employed *in situ* observations of robotic turnovers and team member perception analysis to investigate the barriers to efficient TOT. Foster (11) discusses benchmarks for TOT based on combined data from various ORs in the United States and found the median TOT to be 28.5 minutes. However, an ideal TOT was difficult to establish based on the variability associated with TOT periods. Every hospital has a different system for conducting turnovers which vary by number of staff involved, type of procedure before and after the turnover, and competing interests of team members involved.

The current study of TOT involving surgical robots found that while average TOT was 72 min., staff generally agreed that the TOT should be significantly shorter (e.g., about 33 min.). Interestingly, while none of the staff reported feeling satisfied with TOT, there were differences in perceived contributors to TOT inefficiency and the perceived contributors differed from observed contributors. Specifically, observations highlighted cleaning time as occupying the greatest percent of TOT, while survey responses indicated that the staff perceived time to set up the OR and instrument availability as the greatest barriers.

It is important to understand individual team member perceptions of a given task prior to developing interventions. For example, in a study on role discrepancy, staff who were asked to complete tasks that they perceived to be outside their scope, experienced drops in satisfaction and were more likely to quit their jobs (9,12,13). Moreover, dissatisfied team members can also generate disruptions in OR flow, leading to decreased efficiency and increased TOT (14). The surveys conducted in the current study revealed differences in team member perceptions of TOT. Specifically, team members varied in their

prediction of current TOT, and identification of contributors to inefficient turnover.

When all groups were asked to estimate the current state of turnover, surgeons predicted significantly longer times than other groups. While their prediction was the most accurate to the data observed in this study, it is important to note that perception plays a key role in how surgeons view TOT. In many cases, surgeons leave the OR before the patient is wheeled out of the room, causing them to believe that TOT is actually longer than the actual TOT (15).

With respect to the contributors to inefficient turnover, "time to set up the OR" and "instrument availability" were ranked the highest amongst all team members. Notably, "EVS" which refers to the time required to clean the OR, was considered only the 4th highest contributor, despite actually contributing the greatest amount of observable time. One major challenge that recurred throughout the observation period was the lack of adequate staffing, especially related to EVS. There were several instances where TOT may have been improved if there were more staff available to assist in cleaning.

This study is not without its limitations. Firstly, this project involved a relatively small sample of 20 observable cases collected at a single institution. Additionally, some team members may have altered their normal behavior as a result of being observed, which could skew results towards a faster turnover time (16). However, this source of error is unlikely as previous data demonstrated that our pre-intervention sample of turnovers is similar to that when observers were not present. By observing turnovers, we were able to witness the delays that normally occur in the OR and can help establish strategies to deal with them. Moreover, we found that the pressure to provide a quick and efficient turnover weighed unevenly on each team member involved. Turnover success is interdependent on the team as whole. When a single member does not work in coordination with the team or goals are misaligned, significant delays in TOT are sure to occur no matter how effective the rest of the team is. Another shortcoming of this study was the inability to determine the reason for delays that were not specifically observable or noted in available chart data, and the fact that the role of patients in TOT delay was not addressed (17). Finally, our sample included a variety of robotic surgical procedures. Certain cases required more time for setup or cleaning due to varying levels of complexity, which inherently affected the TOT. However, in the effort to improve all turnovers involving a surgical robot, all cases that occurred were included in this pilot study.

Conclusions

Overall, this study used a human factors approach to identify several opportunities for improvement. Three areas in particular were highlighted for robotic turnover improvement efforts: (1) cleaning time, (2) retrieval of the patient from pre-op and (3) delay from team members on readiness for patient arrival. Next steps will involve multidisciplinary meetings with the staff involved with robotic cases to discuss potential interventions and implementation plans.

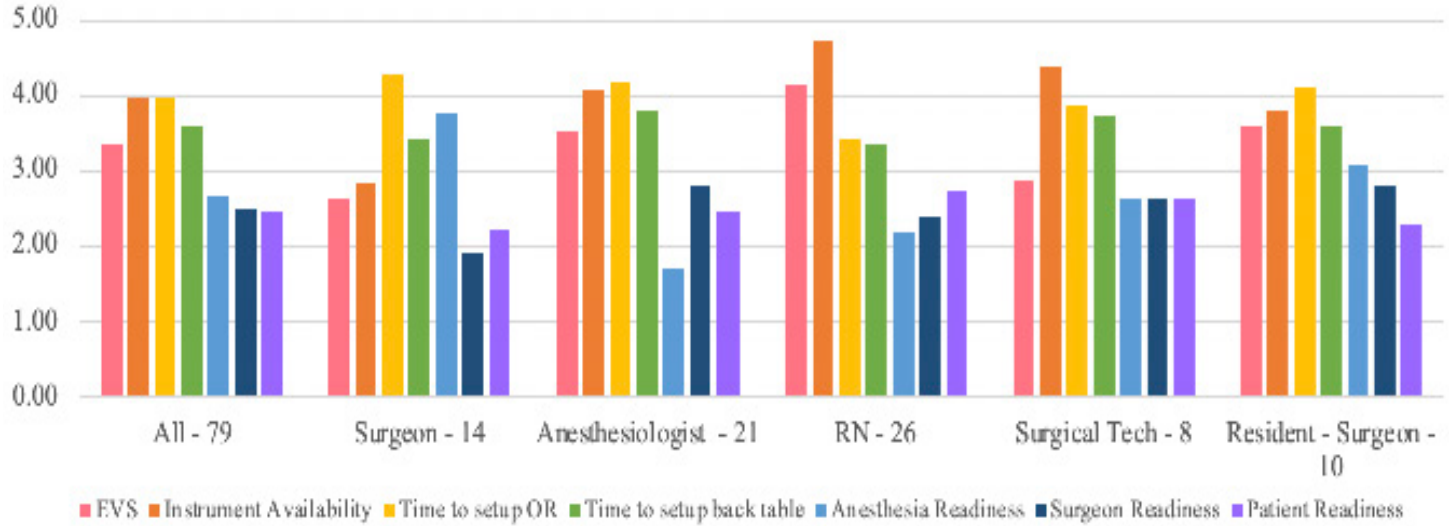

Figure 3: Factors contributing to turnover (1=minor contributor; 5 = major contributor)

Future research on improving TOT during robotic cases should focus on discussing and clearly outlining the requirements for all staff involved in turnover of the previous and following cases. It would also be beneficial to study the effects of establishing a team for each OR on reducing TOT. Having a designated team allows each member to have their roles clearly outlined, and ensures that roles are not altered from case to case. It also helps strengthen the dynamic and cooperation of the team by creating a sense of unity and accountability, which could ultimately lead to more efficient turnover. Another way of instituting a sense of accountability is by providing the OR staff with weekly or monthly reports that indicate the delays and their source.

Ultimately, it is important to objectively critique the current turnover system and to be flexible in seeking improvement, while ensuring that no shortcuts are taken that jeopardize patient health. Setting a benchmark TOT (e.g. 40 mins) might be helpful in establishing a goal for surgeries involving robots. Moreover, reducing TOT has significant implications for hospitals overall because it can lead to improved patient and medical staff satisfaction, as well as economic benefits, without affecting quality of care. A multidisciplinary approach at all levels of the OR and hospital are required to create a cultural change among the staff to optimize the approach to turnovers.

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The Importance of Cadaveric Dissection

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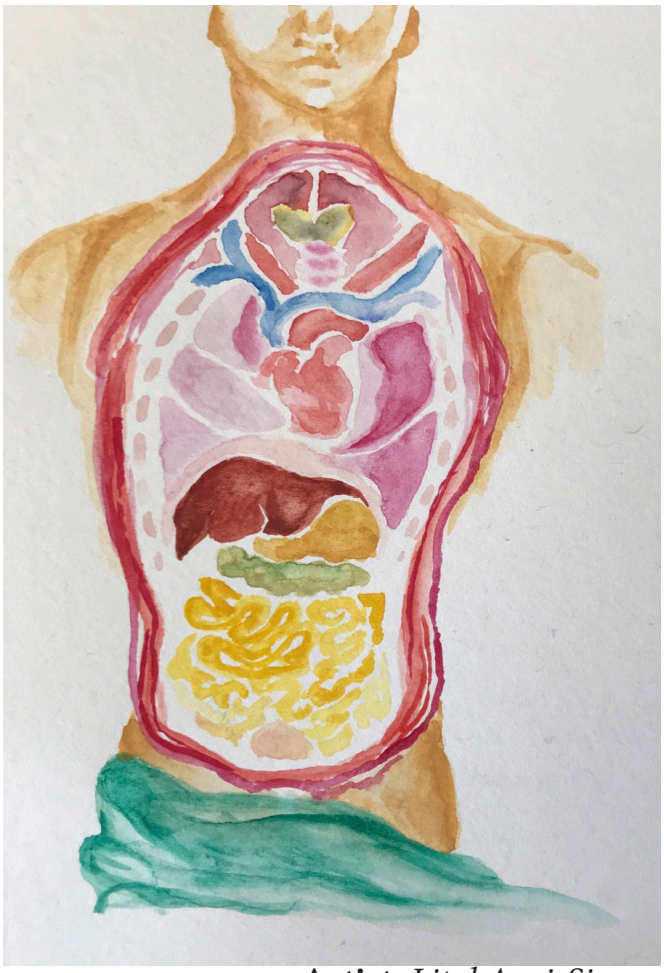

Artist: *Lital Avni-Singer*

Cadaveric dissection has been the cornerstone of anatomical education in medical schools throughout the world for centuries. Recently, some schools have opted to teach anatomy via virtual substitutes. When students reflect on the quality of their learning, many believe the most valuable method of learning human anatomy is through dissection[1]. Students highlight important skills that they attain in the anatomy laboratory, including: teamwork, professionalism and a greater ability to cope with death[1,2]. For many students, even though dissecting a human body provokes anxiety, uneasiness and discomfort, they are still excited about the opportunity and consider it a "rite of passage" in beginning their medical education. Despite the primarily positive experience described by a majority of medical students in the anatomy laboratory, empirical advancements should be made to ensure a deeper, more standardized understanding of gross anatomy by students.

We live in a revolutionary period of educational change. Much of our educational system, including medical studies, is being reimagined through new technology—but, how do these new tools compare with the time-tested techniques of teaching and learning gross anatomy? Students and educators alike marvel at the latest advancements, and it is amazing how much a student may learn about the human body without ever picking up a scalpel, but does newer always mean better?

Last October, Scientific American published an article discussing the utility of virtual reality as a modern substitute for cadaveric dissection[3]. The article quotes James Young, chief academic officer of the Cleveland Clinic, who posits that in the next ten years, traditional cadaveric dissection will become obsolete. But, even given the utility of virtual anatomy tools I argue that these tools cannot replace the value of working with real human tissue.

Through collaborative full-body dissections, students gain a number of unique skills that foster competent and cooperative physicians. Students must learn to work together, integrating theoretical knowledge in order to correctly identify structures and proceed through the dissection. Time in the lab can instill curiosity about the different structures and promotes problem-solving skills. Many students experience working with the deceased for the first time through cadaveric dissection, and have the opportunity to become more comfortable with death, something many physicians struggle with throughout their careers.[4]—Collaborative cadaveric dissection

can also foster professionalism, as students must face difficult and intimate facets of medical-work early-on in their medical education.

VR dissection is not without merit; it provides a clean and straightforward method for understanding the human body. And yet, this simplicity avoids a key concept which students learn in the anatomy lab: the human body is messy. Finding structures requires specialized knowledge, precision and patience—it is not (and should not be) as simple as typing into a search bar. And furthermore, each body is different—discovering anatomical anomalies in the lab is an exciting aspect of learning in the anatomy lab. Through these detections, students see first-hand the importance of patient-focused medicine. If we teach anatomy with a "cookie-cutter" approach, we risk conveying that it is okay to approach patients in the same manner.

That being said, I do believe that there is a place for simulated electronic anatomy education. The utility of these tools is immeasurable and certain advancements provide students with perspectives that otherwise may be unattainable. However, these new tools should be used to supplement rather than substitute cadaveric dissection. Indeed, studies have shown that a multi-modal approach is the most effective way for students to learn anatomy.[5]

While the benefit of cadaveric dissection is clear, there is room for improvement to both instruction and learning. According to the existing literature focused on the student perspective, anatomical-education varies widely both between and within institutions. This variation is likely due in part to differing learning styles, and also results from discrepancies between student-preparation and logistical aspects of the time in the anatomy laboratory. Much of the research has focused on the utility of dissection, but little emphasis has been placed on eliciting the most effective way for students to benefit from the experience. For example, there is currently no uniform standard across American medical schools for introducing and preparing students for their first dissection. Moreover, the number of students assigned to a specific cadaver varies widely, as does the quality and variety of tools available, and the amount of supervision and instruction from trained laboratory personnel.

Through reassessing and fine-tuning the specific components of dissection-education, I believe that it is possible to foster a more universally positive experience for medical students learning gross anatomy. Improving the experience of anatomy education will allow for more integrated long-term learning that will lead to more competent, patient-centred physicians.

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A Complex Case Presentation on Double Depression and Personality Disorder

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Abstract

The purpose of this case report is to demonstrate the complexity of diagnosing and treating depression. This case involves a female with an intricate past psychiatric history, who has been hospitalized for suicidality subsequent to her pregnancy losses. Because her lengthy timeline of depression is overlaid with episodes of severe depression, she was investigated for double depression. Her internal response to her depression, hospitalization, and treatment are concerning and suggestive of a personality disorder which further complicates the diagnosis and the treatment of this patient.

Introduction and definitions

Psychiatric conditions come in different varieties, each with a unique and different presentation. Consequently, diagnosing is a challenging task despite having existing guidelines. There are various treatment options for psychiatric disorders ranging from medication, to behavioral therapy, and electroshock therapy. Treatment varies greatly from patient to patient and is very reliant on the severity and presentation of the patient's condition. Usually a personalized cocktail of these therapies is administered to each patient.

According to the DSM-5 criteria[1], a diagnosis of major depressive disorder (MDD) requires five of the following for a period of two consecutive weeks: depressed mood; diminished interest in activities; significant change in appetite or weight; insomnia or hypersomnia; psychomotor agitation or retardation; fatigue to decreased energy; feelings of worthlessness or inappropriate guilt; diminished concentration; suicidality.

One of the symptoms must be depressed mood or loss of interest and the episodes cannot include mania. Additionally, the symptoms must cause clinically significant distress or change in function and the episode cannot be attributable to a substance or medical condition[1]. First line treatment for MDD is a selective serotonin reuptake inhibitor (SSRI) or a selective norepinephrine reuptake inhibitor (SNRI). Cases of depression that are severe or refractory to pharmaceutical treatment can be treated with electroconvulsive therapy (ECT), which involves an induced generalized seizure under anesthesia.

Similar to MDD, persistent depressive disorder, or dysthymic disorder, requires the same criteria for diagnosis. However, the symptoms need to be present for at least for two years without an asymptomatic period of no more than two months.

Adjustment disorder with depressed mood can also present similarly to MDD[2]. The key difference is that adjustment disorder does not meet the DSM-5 criteria for MDD diagnosis. Instead, its diagnosis is that of exclusion and the disorder must arise within three months of the onset of a stressor.

The presence of personality disorders in patients can complicate the diagnosis and inevitably the treatment of the patient. Personality disorders are defined by characteristics and thought processes that affect a patient's mannerisms and social interactions[1]. They can be divided into three clusters: A, B, and C. Cluster B disorders, which are more relevant to this case report, include borderline personality disorder. Borderline personality disorder is associated with unstable mood and relationships, along with impulsive self-harm. Other cluster B disorders, such as narcissistic and histrionic personality disorders, are also strongly associated with mood fluctuations. Typically, personality disorders are treated with cognitive behavior therapy (CBT), which is meant to help the patient navigate their emotions. However, borderline personality disorder is treated specifically with dialectic behavioral therapy (DBT), which more heavily targets a patient's behaviors and relationships.

Identification: MF is a 39-year-old female born in Israel. Prior to admission, she lived in Kadima, Israel with her husband and two children. She has an administrative job at Clalit and is currently on leave of absence. Her native language is Hebrew and English is her second language.

Chief Complaint: The patient was admitted upon her will to Lev HaSharon Mental Health Center by referral from her psychiatrist upon disclosure of a suicide attempt by method of ingesting 10 Clonex (clonazepam) pills.

Presenting Illness: MF presented at the hospital after a suicide attempt triggered by depression. Two months prior, the patient had an elective abortion of her fourth pregnancy due to abnormal amniocentesis results. It took the patient two months for her feelings of guilt, remorse, and sadness to develop. When the depression peaked, she ingested 10 of her husband's Clonex (clonazepam) pills. She had no adverse effects other than deep sleep. Upon disclosure of this experience to her psychiatrist of 5 years, she was admitted to the closed ward at Lev HaSharon willingly.

Post-abortion and pre-hospitalization, the patient was on maternity leave from work. During this time, she would watch pre-recorded episodes of the TV show "One Born Every Minute", a TV show that follows pregnant women and their labor and delivery. She reports to having stayed in bed, binge watching this show until it was time for her to pick up her kids from school.

During her current hospitalization, the patient notes suicidal thoughts are always present and fluctuate in intensity throughout the day. She also reports having slept poorly during the night, initially due to a disturbing roommate and later due to restlessness and having a poor appetite at the hospital. She believes that if she died, her husband could obtain a better wife and her children a better mother. She also notes that there is not much to her to love because she lacks happiness and doesn't have the energy to take care of her kids. Despite having these thoughts, she does not have a current plan to commit for suicide during the hospitalization. She comments that her depressed mood is also constant, but some days are worse than others. The patient's husband, parents, and siblings visit her in the ward. After being transferred to the open ward, she has had the opportunity to visit home over the past two weekends. She reported to have enjoyed her time with her kids, husband, and family and to have eaten better.

The patient started off in the closed ward and was subsequently moved to the open ward. The patient was reactive to treatment as per her own self-reflection. Pre-ECT therapy and during her early hospitalization, she expressed that she didn't see herself getting out of her depression and could not see what the future of her condition held. Post-ECT therapy and another week into her hospitalization, she expressed improvement and had some hope about her depression.

Despite having two eventful pregnancies, MF desired a third child when she returns home. She was unbothered by the potential consequences that another pregnancy could have on her condition. She

was unsure whether to name her next child the name she had initially chosen for her aborted child.

Past Psychiatric History: MF's first exposure to psychiatric care was in her first year of university. Her stress and frustration in university stemmed from trying very hard in school, but not attaining the results she desired. She started seeing the university psychiatrist and was treated for her depression. She was started on SSRI and SNRI therapy which she continued to take consistently. Throughout her treatment she cycled through Recital (citalopram), Paxcil (paroxetine), Lustral (sertraline), and Effexor (venlafaxine). She was also given 0.5 mg Risperdal (risperidone), an anti-psychotic, for augmentation therapy which was later upped to 3mg.

As a consequence of her depression and stress, the patient's appetite in university decreased and she started losing weight. The psychiatrist she was seeing recommended that she be hospitalized at Tel HaShomer in 2003, during which she was diagnosed with anorexia and borderline personality disorder, as she was found to have self-inflicted cuts on her leg. She was hospitalized for 3.5 months, after which she sought treatment from a private psychiatrist. She fully recovered in 2007.

In 2012, the patient had a miscarriage at 2 months of gestation. Three months after her miscarriage, she suffered from severe depression which triggered her to purchase rat poison. When asked why she didn't ingest the poison, she reported she didn't have the time and was "scared of the pain." She was admitted to the open ward at Lev HaSharon for treatment due to suicidal ideation and formulation of a plan. During this hospitalization, it was found that she was pregnant again. During her 9 months of pregnancy, the patient was kept in the open ward at Lev HaSharon to help her cope with the pregnancy and prepare her for motherhood. She recounts that the experience at the hospital was helpful to her and her delivery and postpartum experience were uneventful.

Past Medical History: The patient is diagnosed with essential tremor for which she takes no medication after having tried several ineffective treatment options. The patient has been diagnosed with anorexia and borderline personality disorder in the past.

Family History: The patient denies any family history of a psychiatric nature. Her grandfather was diagnosed with essential tremor.

MF's parents are still married and live in Tel Aviv. She is third of three siblings, who are 5 and 7 years older and live in Ra'anana and Herzaliya respectively. As a result of the age difference, she notes they were not very close but have a standard cordial relationship. She also notes she was not very close to her parents growing up, but they still see each other and talk on the phone often. Her parents and her sister visit her at the hospital during her hospitalization.

MF is married with 2 kids, a daughter and son, 6 and 3 years of age respectively. She met her husband through mutual friends and comments that they have a very good relationship. He visits her in the hospital and is cordial with the hospital staff. During her hospitalization, he takes care of the children while also continuing to work. MF is concerned that her children miss her during her hospitalization and has told them she is on a business trip.

Personal and Social History:

Childhood: MF grew up in a nonreligious household. The patient describes her childhood as normal, but recounts she didn't have many close friends.

Adolescence and Young Adulthood: The patient completed two years of army service as a sergeant in communication. She completed her undergraduate degree in biology in Israel, then went on to pursue a master's degree in 2006 in Social Sciences and Human Affairs in Rome, and later a second master's degree in Healthcare Management in Israel.

Adulthood: The patient has been married since 2009 and has two children. She reports her marriage is "good." She currently works at an administrative job at Clalit and is currently on leave of absence. She enjoys her master's degree in Healthcare Management very much but doesn't feel that her current job meets her expectations. She is unsure whether she will continue to pursue her career after this hospitalization

She recognizes that she is nonreligious, even more so from her childhood. She notes she does not prefer identifying with religion because of all the conflict it has caused in the present day news. She does not attribute her atheist lifestyle to her depression or

to having lost two of her pregnancies.

Patient denies alcohol use, but has used drugs recreationally a few times in university. Patient smokes, but only during hospitalizations due to "boredom."

MSE:

Appearance: The patient appears her age; she is dressed appropriately to the season and has good hygiene.

Psychomotor Activity: The patient has essential tremor in her hands, but does not display any other psychomotor agitation.

Cooperation: The patient is actively cooperative, answers questions to her best ability and did not avoid any questions.

Consciousness: The patient is oriented to person, place, and time.

Speech: Her speech is normal but slightly monotonous. Her tone is moderately reactive upon discussing heavier emotions such as her suicide and her children.

Affect: The patient predominantly seems euthymic. However, often times her affect did not match the depression and other emotions she was describing. She is very indifferent towards her suicidality and depression

Thought process: The patient's thought process is linear and she stays on topic persistently.

Thought content: The patient's thought content is nihilistic. She believes that her husband and children would benefit from a new wife and mother if she were to die.

Mood: The patient expresses feelings of sadness, guilt, hopelessness, frustration and tiredness.

Suicidality: She expresses that she has consistent thoughts of suicide that "come and go."

Perception: The patient denies hallucinations.

Cognition: The patient has intact cognition. She is able to recount dates and events appropriately.

Insight: The patient does have a relative amount of insight into her condition. She was willfully hospitalized and takes her medication consistently. It is clear she understands that she is depressed, as she vocalizes it. However, MF is emotionally detached and doesn't fully understand how losing a child is influencing her. She may have insight into her condition intellectually, but she lacks psychological and emotional insight.

Judgement of reality: The patient has proper judgement of reality.

Judgement: The patient has acted appropriately during all the interviews and answered all questions as per requested. Because she wants to be hospitalized and understands the seriousness of her illness and is not resisting help, her judgement can be described to be intact. Had she been resistant to treatment, her judgement might be considered impaired.

Medications:

MF's current medications are Aripri (aripiprazole), 300 mg Favoxil (fluvoxamine), 0.5 mg Lorivan (lorazepam), 25 mg Seroquel (quetiapine) SOS to be used during periods of anxiety. During her hospitalization, the patient was started on 25 mg Lamictal (lamotrogine), to augment the effect of her SSRI. The patient also pursued ECT therapy. Lamictal was stopped prior to the ECT in order to assess the improvement of her depression and ensure any fluctuations in her condition is properly attributed to the effect of the ECT.

Summary and Discussion

MF is a complex patient. She was diagnosed with a major depressive episode during this hospitalization. The differential diagnosis for this patient is also complicated. As the patient's last two hospitalizations and suicidal plans precipitated after a life changing events, adjustment disorder is a diagnosis to consider[2]. However, since the patient meets the criteria for depression, adjustment disorder is less likely.

The patient has a history of depression from university, a period longer than 2 years, which raises suspicion for dysthymic disorder. MF's severe depressive episode after her abortion, and also previously in 2012 after her miscarriage, is overlaid on

top of a baseline depressed state which could also be interpreted as an exacerbation of her dysthymic disorder. This complexity could be attributed to double depression.

MF should continue her medication 10 mg Aripri (aripiprazole), 300 mg Favoxil (fluvoxamine), 0.5 mg Lorivan (lorazepam), 25 mg Seroquel (quetiapine) SOS. She should also continue her ECT treatment and be monitored for improvement. Upon thorough and periodical evaluation of her depression and suicidality, and if she desires, she can be discharged from the open ward and continue day treatment.

A concerning quality that MF elicits is indifference to her depression and minimization of her suicidality. When questioned about this, she noted "I have always been this way." This comment raised the suspicion that MF has some personality traits that may be attributed to her baseline depressed state. The patient was diagnosed with borderline personality in 2003 when she was hospitalized for anorexia. However, she was very young then and since her 2003 hospitalization, she could have undergone personal growth. Currently, she is functional and has been in stable, healthy relationships with her husband, parents, and sisters for many years. These characteristics deflect from the diagnosis of borderline personality disorder. Another concerning aspect of MF is her nihilistic behavior. She has been consistent in expressing that she believes her husband and children would be better off without her. Perhaps this could also be attributed to some of the personality traits that are also influencing her baseline depressed state. Further multiple and holistic evaluations would be necessary for a diagnosis of a personality disorder.

Apart from being suggestive of personality traits, MF's indifference and nihilistic attitude are concerning aspects of her condition. It is indicative that she is numb to her situation and has a warped way of thinking that is impairing her from genuinely understanding how her depression is affecting her on a more intricate level. As a result, she also struggles to fully understand the implicated risks of her desire to have another child post-hospitalization.

What should be necessary and helpful for the patient in the long run is some form of psychotherapy. As she has a desire to have another child, she needs to understand the consequences and risks of the pregnancy and be able to evaluate herself to determine if she can handle the stressors. This could potentially utilize desensitization and exposure therapy. Additionally, if the patient has a personality component to her diagnosis, it would be beneficial to start DBT, for a borderline personality disorder, or CBT for other personality disorders. Family therapy could also be beneficial to help address the patient's nihilistic thoughts.

Conclusion

The DSM-5 criteria are important in navigating between the small nuances of psychiatric conditions. It is important to consider that psychiatric patients often cannot be boxed into a single diagnosis. Patients must be regarded holistically and evaluated in all areas of their life and past. In the scenario of MF for example, treating her current suicidality could help stabilize her mental health acutely. From a long-term perspective, including her psychiatric history since her late teens and her previous episodes of suicide and self harm, her condition is now more complex and severe. Proper follow up care is a vital part of a patient's treatment to ensure it is effective and that the patient is adherent. Additionally, evaluation of the patient's insight into their condition and their evolving understanding of their illness is an important part of understanding a patient's improvement. MF's case is one example of how intricate cases of depression can be, with many different factors such as her personality disorder, that influence her treatment and her attitude towards her depression. Such a presentation requires a treatment that targets the roots of all her issues and blends various treatment techniques including medication, behavioral therapy and ECT.

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Doctor, what should I eat?

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The gut microbiome is an extremely trendy topic. A simple search on Instagram, one of today's leading social media platforms, will show around 27,000 posts, in contrast to the 20,000 PubMed results for the same keyword. While science and medicine have always extended into mainstream society and popular culture, the number of people talking about the bacteria living in our intestines is impressive.

So, what is the gut microbiome? The gut microbiome is the collection of "good bacteria" that live symbiotically in our intestinal tracts.[1]an in-depth review of the literature was undertaken to evaluate the major contributors to potential changes in the gut microbiota and their corresponding sequelae, and to determine if consuming LNCS (e.g., acesulfame K, aspartame, cyclamate, neotame, saccharin, sucralose, steviol glycosides We give them a home and in turn, they help us break down food and absorb nutrients. Beyond digestion and nourishment, the gut microbiome helps us modulate our immune systems and regulate our moods. These bacterial populations can even outcompete malignant microorganisms, like Clostridioides difficile, protecting us from harmful bugs.

Gut microbiome research has also shed immense light on the debate regarding non-caloric sweeteners. Unlike conventional sugars, non-caloric sweeteners were once thought to be harmless. However, the effects of non-caloric sweeteners on the gut microbiome have recently attracted attention. One theory is that eating non-caloric sweeteners exerts selective pressure on sugar-hungry bacterial subpopulations, which then signal for host cravings of both non-caloric and traditional sugars. Ironically, zero-calorie sweeteners actually cause us to overeat all types of sugars, gain weight, and even develop diabetes in the long run.[1]an in-depth review of the literature was undertaken to evaluate the major contributors to potential changes in the gut microbiota and their corresponding sequelae, and to determine if consuming LNCS (e.g., acesulfame K, aspartame, cyclamate, neotame, saccharin, sucralose, steviol glycosides You really are what you eat.

For as much investigation as there is into the gut microbiome's healthful function, there is equally as much into how easily it can be threatened. This focus on protecting the gut microbiome is particularly important when treating patients with conditions such as diabetes mellitus, Crohn's disease, and ulcerative colitis. Not only do these diseases involve metabolic and digestive factors, but also biopsychosocial components conferred by a healthy gut microbiome.

One growing area of interest is the gut microbiome's implication in mood regulation. Our gastrointestinal tracts are sometimes referred to as our "second brain," given that around 90% of our serotonin is created in the intestines. Research has described the intimate relationship between diet, gut microbiota, and mood disorders,[2] and has prompted the question of the gut microbiome's contribution as an antidepressant. For example, rats who received microbiota transplants from human patients with major depressive disorder began experiencing depressive symptoms.[3] As well, rats who were stressed to induce depressive symptoms showed a reduction in both number and populations of microbiota.[3]including major depressive disorder (MDD These findings suggest a bidirectionality that has been referred to as the mind-body-connection.

Nowadays, patients are increasingly health literate and will expect us, as future medical professionals, to give them nutrition recommendations. Medical professionals need to be informed for every patient, more than just the "classic" gastrointestinal or metabolic patients. For example, the millennial generation are a group that is particularly interested in food and food-related decisions, considering that they spend more than any previous generation in that sector.[4]

We are living in a time and culture that is preoccupied with what we eat. On one hand, this engrossment is better than the faulty notion we once had about carbohydrates being equal regardless of their source. On the other hand, the gut microbiome's rise to celebrity and our generation's obsession with food are signs that people may be hungry for answers

we cannot satisfy. British food writer Nigella Lawson perfectly captures the millennial relationship with food in her book How to Eat:

> *"What I hate is this new age voodoo about eating, the notion that foods are either harmful or healing, that a good diet makes a good person and that that person is necessarily lean, lumber, toned and fit… such a view seems to me in danger of fusing Nazism (with its ideological cult of physical perfection) and puritanism (with its horror of the flesh and belief in salvation through denial)"*[5]

So, what do we do when our friends and family ask us about what to eat? How about when our patients inevitably do? While we can make some recommendations rather confidently, we might be underprepared for our duties. We receive minimal diet and nutrition training through medical school and residency,[6] putting us at a disadvantage; we are underinformed when talking to patients about dietary topics in which they are well-versed. From Paleo, to Atkins, to the Ketogenic diet, we must know the risks and benefits of each and how they may affect the patient sitting in front of us. Certainly, we can and should learn more. The real challenge, however, lies in satisfying the cultural and generational preoccupation with nutrition and the loaded questions that come with it.

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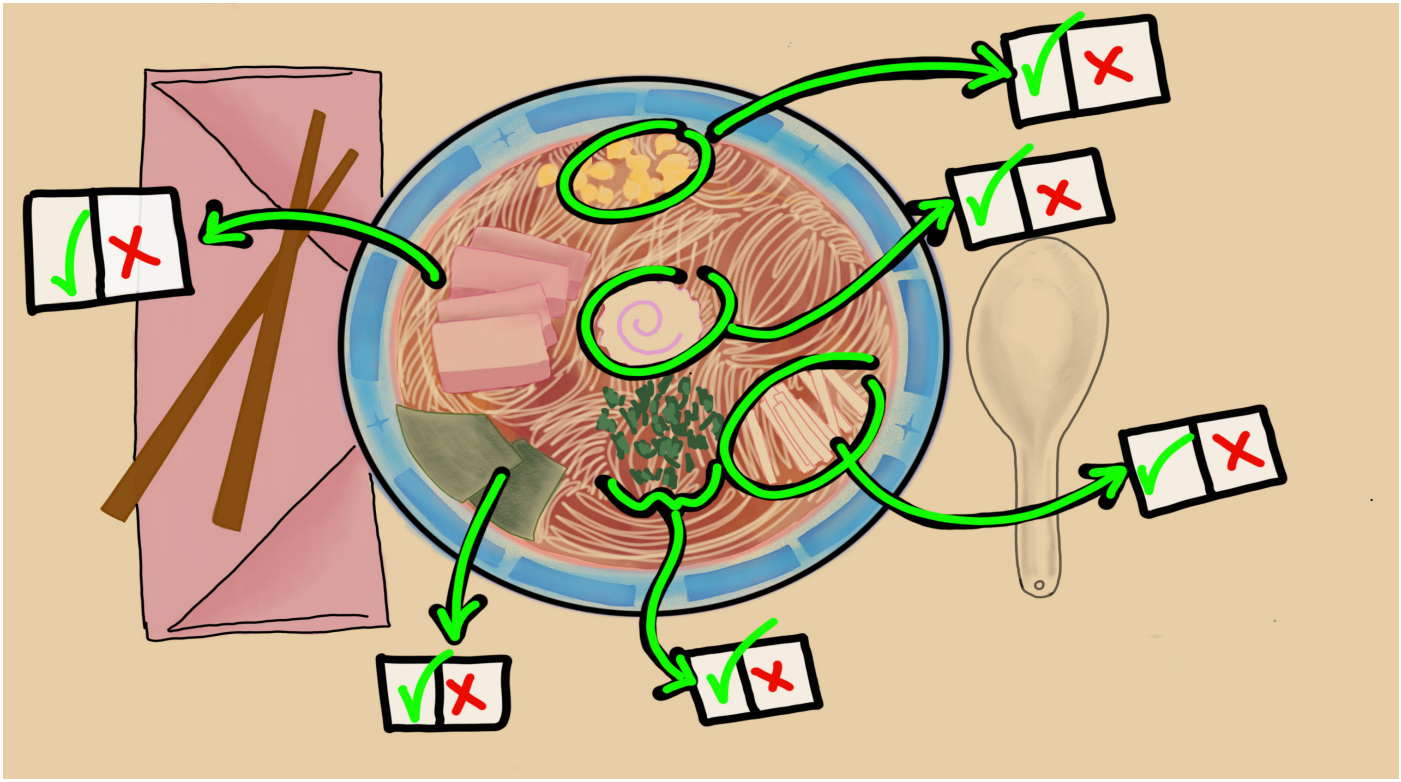

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ORIGINAL RESEARCH

MitraClip in the Setting of Cardiogenic Shock

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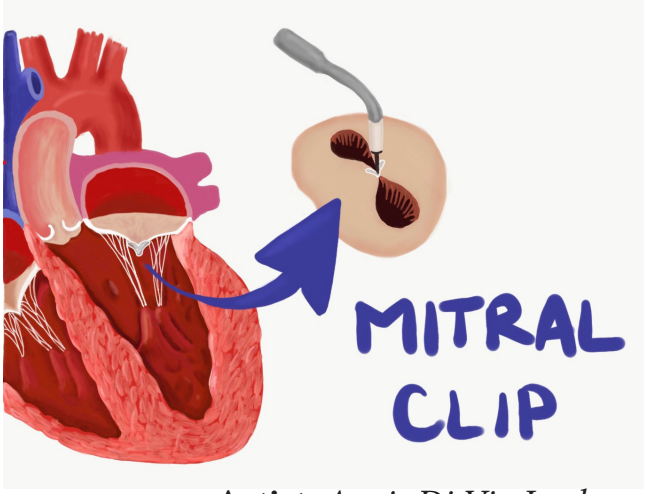

Artist: *Anais Di Via Ioschpe*

Introduction

The use of MitraClip for the treatment of severe mitral regurgitation (MR) has been well studied in medically optimized patients. However, little is known about its use in the setting of cardiogenic shock (Franzen, 2014). While the reduction in regurgitant volume may in theory improve cardiogenic shock by improving forward cardiac output, providers must balance this with the inherent risk of the procedure. We sought to assess the short- and long-term outcomes of patients undergoing MitraClip for severe MR in the setting of cardiogenic shock.

Materials and Methods

We performed a retrospective observational cohort study of patients who underwent MitraClip at a large academic institution between 2013 and 2019. Patient charts were reviewed to identify patients with pre-procedure cardiogenic shock. Patients were considered as having cardiogenic shock if at least one of the following criteria were present: 1) documentation of ongoing cardiogenic shock by a provider, 2) hemodynamic monitoring data (cardiac index <2.2), or 3) use of inotropes (Dobutamine, Milrinone or Dopamine) or vasopressors (Norepinephrine, Epinephrine or Vasopressin) within 24 hours of the procedure. Patients were excluded if they lacked a pre- or post-procedure echocardiogram.

Results

Out of 448 eligible MitraClip patients, 29 (6.5%) were identified as having pre-procedure cardiogenic shock. Compared with patients undergoing MitraClip without cardiogenic shock, patients with cardiogenic shock were younger (77.0 ± 12.0 vs 66.5 ± 16.4, p = 0.001), more frequently male (57.3% vs 79.3%, p=0.02) and had a lower left ventricular ejection fraction (48.1% vs 35.8%, p=0.004).

On pre-procedure echocardiography, MR severity was graded as severe or very severe in 21 (72.4%) of those with cardiogenic shock and 301 (71.8%) of those without shock. Of these patients, MR severity was reduced to moderate or less in 26 (89.7%) of those with shock and 400 (95.5%) of those without shock following the procedure.

Table 1: Demographics and Clinical Characteristics

	Shock Patients	Non-shock Patients	p-Value
	Demographics		
Age at time of procedure	66.52 ± 16.39	77.0 ± 12.0	.001
Male n (%)	23 (79.3%)	240 (57.3%)	0.020
Race n (%)			0.290
White	24 (82.76%)	352 (84.01%)	
Black	1 (3.45%)	34 (8.11%)	
Asian	4 (13.79%)	27 (6.44%)	
American Indian/Alaskan Native	0 (0%)	1 (0.24%)	
Native Hawaiian/Pacific Islander	1 (3.45%)	5 (1.19%)	
	Echocardiographic Parameters		
Left Ventricular Ejection Fraction (%)	35.79% ± 22.98	48.12% ± 19.31	0.004
Left Ventricular Diastolic Diameter (cm)	5.8 ± 1.08	5.4 ± 1.1	0.968
LV diameter Systole (cm)	4.7 ± 1.56	4.07 ± 1.37	0.978
Severity of MR by TEE			
None	0 (0%)	0 (0%)	
Trace/Trivial	0 (0%)	0 (0%)	
Mild	1 (3.45%)	3 (0.72%)	
Mild-Moderate	0 (0%)	0 (0%)	
Moderate	2 (6.90%)	36 (8.60%)	
Moderate-Severe	5 (17.24%)	79 (18.85%)	
Severe	20 68.97%)	301 (71.84%)	
Very Severe	1 (3.45%)	0 (0%)	
Mitral Valve Mean Gradient (mmHg)	4.4 ± 2.47	3.06 ± 1.67	0.996
	Clinical Variables		
Inotropes n (%)	26 (89.66%)	-	
Dobutamine	23 (79.31%)	-	
Dopamine	12 (41.38%)	-	
Milrinone	7 (24.14%)	-	
Number of Inotropes n (%)		-	
0 inotropes	3 (10.34%)	-	
1 inotrope	13 (44.83%)	-	
2 inotropes	10 (34.48%)	-	
3 inotropes	3 (10.34%)	-	
Pressers n (%)	16 (55.17%)	-	

Table 2: Procedural Variables and Clinical Outcomes

	Shock Patients	Non-shock Patients	p-Value
Number of clips	1.28 ± 0.59	1.19 ± 0.49	0.786
	Echocardiographic Parameters		
EF	30.83 ± 19.36	46.46 ± 17.58	<0.001
LV diameter Diastole (cm)	6.1 ± 1.2	5.21 ± 1.07	0.999
LV diameter Systole (cm)	5.3 ± 1.23	3.97 ± 1.29	1.0
MV mean gradient	4.1 ± 1.73	4.23 ± 2.01	0.349
Severity of MR by TEE			
None	1 (3.45%)	3 (0.72%)	
Trace/Trivial	4 (13.79%)	37 (8.83%)	
Mild	12 (41.38%)	244 (58.23%)	
Mild-Moderate	4 (13.79%)	0 (0%)	
Moderate	5 (17.24%)	116 (27.68%)	
Moderate-Severe	0 (0%)	11 (2.62%)	
Severe	2 (7.90%)	8 (1.91%)	
Very Severe	0 (0%)	0 (0%)	
Patients whose MR Severity Decreased Post-Procedure	86.21%*	95.94%	0.016
	Clinical Variables		
On inotropes n (%)	22 (75.86%)	-	
Dobutamine	20 (68.97%)	-	
Dopamine	9 (31.03%)	-	
Milrinone	4 (13.79%)	-	
Inotropes n (%)		-	
0 inotropes	7 (24.14%)	-	
1 inotrope	13 (44.83%)	-	
2 inotropes	7 (24.14%)	-	
3 inotropes	2 (6.90%)	-	
Patients who Decreased # of Inotropes Post-Procedure n (%)	8 (27.59%)	-	
Vasopressors n (%)	15 (51.72%)	-	
Deaths n (%)			
Death in Lab	0 (0%)	0 (0%)	
Death within 30 days of procedure	6 (20.69%)	0 (0%)	<0.001
Deaths or Re-hospitalizations within 30 days n (%)	7 (24.14%)	30 (7.16%)	0.0013

*One patient in whom post-procedure mitral regurgitation severity could not be assessed.

Of the patients in cardiogenic shock, 26 (90%) were on inotropes and 16 (55%) were on vasopressors. While not statistically significant, it was found that within one day of MitraClip procedure, the rates of inotrope and vasopressor requirements decreased to 22 (76%) and 16 (55%), respectively.

Mortality 30 days post-procedure was 20.7% (6 patients) for shock patients, compared with 0% in those without shock ($p<0.001$). At 1-year post procedure, mortality was 41.4% (12 patients) and 0.24% (1 patient) for those with shock and without shock, respectively ($p<0.001$). Further, the 30 day composite outcome of mortality and re-hospitalization was more common in the group with shock than in the non-shock group(24.1% vs 7.2%, p=0.001).

Discussion

Overall, our results showed that MitraClip significantly reduced the severity of mitral regurgitation. This improvement in regurgitation severity was particularly prominent in the patients with cardiogenic shock. Additionally, the results show that use of MitraClip reduced the need for inotropes and vasopressors in patients with cardiogenic shock. Taken together, these results support the conclusion that MitraClip in the setting of cardiogenic shock is feasible. This is promising for long-term outcomes in patients in cardiogenic shock with mitral regurgitation.

However, readmission rates and mortality rates remain high. While the reduction in regurgitant volume may in theory improve cardiogenic shock through improved forward cardiac output, providers must balance this with the inherent risk of the procedure.

Prospective studies are needed to determine if MitraClip in the setting of cardiogenic shock offers benefits over medical therapy alone. Ongoing research is needed to determine the effect of MitraClip on mortality rates, as well as on re-hospitalization rates. While short-term mortality rates seem to decrease following MitraClip, long-term results require follow-up that has not yet been evaluated.

Figure 1: Change in Severity of Mitral Regurgitation from Pre to Post-Procedure

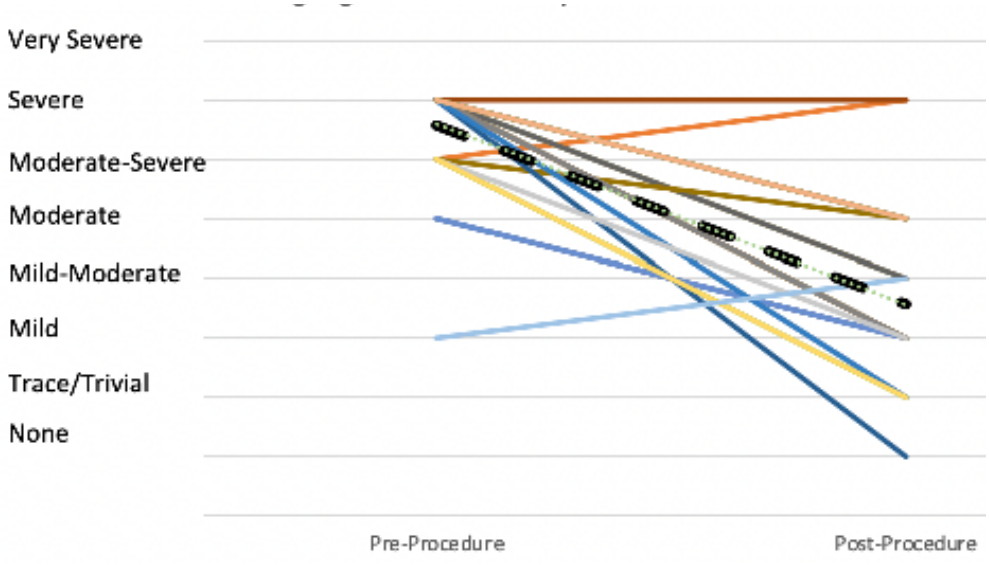

Figure 2: Change in Number of Inotropic Agents from Pre to Post-Procedure for patients with Pre-Procedure Cardiogenic Shock

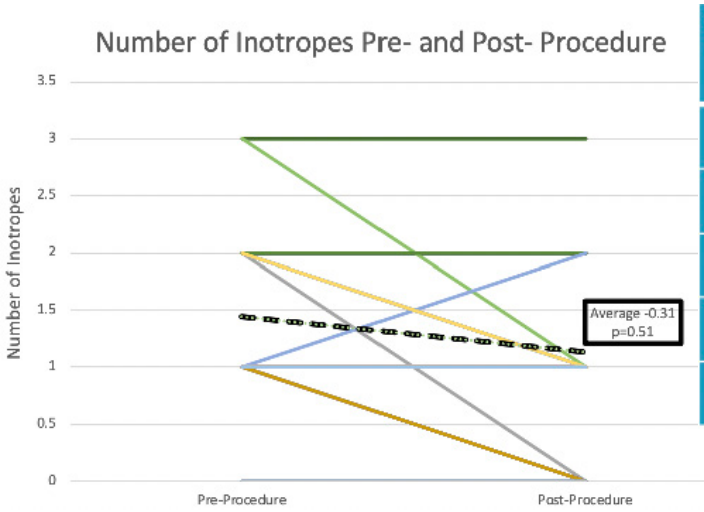

Figure 3: Inotrope and vasopressor requirements in cardiogenic shock patients pre-procedure

# of inotropes Pre-procedure	# Shock patients
0 inotropes	3 patients
1 inotrope	13 patients
2 inotropes	10 patients
3 inotropes	3 patients
Any inotrope support %	90%

Inotropes include: dobutamine, milrinone, doputamine

# of vasopressors Pre-procedure	# Shock patients
0 vasopressors	13 patients
1 vasopressor	16 patients
2 vasopressors	0 patients
3 vasopressors	0 patients
Any vasopressor support %	55%

vasopressors include: norepinephrine, epinephrine, vasopressin

90% of patients on at least 1 inotrope pre-procedure
55% of patients on at least 1 vasopressor pre-procedure

Limitations of the study include missing mortality data, errors in chart documentation, non-blinding of research associates, and the limits of retrospective design.

Conclusion

Use of MitralClip for the treatment of MR in the setting of cardiogenic shock is feasible, with noted reductions in the severity of MR and trends towards reduced inotropic requirements. However, readmissions and mortality rates remain high. Prospective studies are needed to determine if MitraClip in the setting of cardiogenic shock offers a benefit over medical therapy alone.

Figure 4: Inotrope and vasopressor requirements in cardiogenic shock patients post-procedure

# of inotropes Pre-procedure	# Shock patients
0 inotropes	7 patients
1 inotrope	13 patients
2 inotropes	7 patients
3 inotropes	2 patients
Any inotrope support %	76%

Inotropes include: dobutamine, milrinone, doputamine

# of vasopressors Pre-procedure	# Shock patients
0 vasopressors	14 patients
1 vasopressor	15 patients
2 vasopressors	0 patients
3 vasopressors	0 patients
Any vasopressor support %	52%

vasopressors include: norepinephrine, epinephrine, vasopressin

76% of patients on at least 1 inotrope post-procedure
52% of patients on at least 1 vasopressor post-procedure

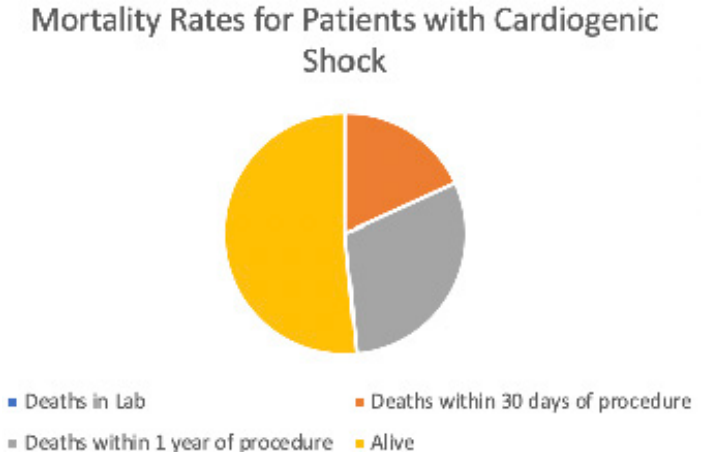

Figure 5: Mortality Outcomes following MitraClip for Patients in Cardiogenic Shock

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Frailty for the Medical Student

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Thanks to the advances of modern medicine, more people are living longer. As more people are aging, we need to shift our focus from healing the patient's disease to seeing the patient's life as a whole. For the older adult, it becomes less about medical fixes, and more about ensuring quality of life. One of the emerging paradigms to consider in the elderly population is the concept of frailty. Frailty is an increasingly popular model, recently defined in the New York Times as "an accumulation of problems that leave the patient vulnerable to stressors".[1] In broad strokes, it is the idea that when comparing two individuals of the same age, one might appear 'older' than the other—weaker, more ill, less mobile, and more hindered by their age.

In the past, assessments to measure frailty were solely carried out by geriatricians. However, it is increasingly being integrated in other fields, such as by surgeons during their pre-surgical assessments. There is a movement to consider the patient as a whole when evaluating candidacy for any therapy or procedure, even ones considered low-risk or routine. A recent article in JAMA Surgery demonstrated that older adults are more likely to die following minor procedures, even if the procedure goes well.[2] The concepts of specialized elder care are starting to be integrated into medical school curricula.[1] However, without being taught specifically, medical students will not have an understanding of frailty as a concept and how to manage this patient population.[3] The aim of this article is to give a brief introduction to the concept of frailty, explain how it is measured, and underscore its significance to future medical practice.

What is Frailty?

Frailty is a geriatric syndrome that increases an individual's vulnerability to physiological stressors, such as acute or chronic disease and iatrogenic stressors.[4] This syndrome arises from an imbalance in multiple physiological systems that leads to a decline in homeostasis, and represents the difference between chronological age and biological age.[5] The Frailty phenotype is characterized by low physical activity, weakness, exhaustion, slowness, and weight loss.[6] Frailty can also be characterized as an accumulation of health deficits, such as comorbidities and disabilities.[7] The pathophysiology of frailty involves the deregulation of the immune, hormone, and endocrine systems, notably upregulation of inflammatory cytokines such as interleukin-6 and C-reactive protein, decreased testosterone levels, and insulin resistance.[8,9]

The age-associated activation of inflammatory cells and decreased androgen levels upsets the balance between anabolic and catabolic stimuli, causing muscle breakdown and exacerbating the effect of aging on protein metabolism.[8,10,11] This progressive decline in muscle mass and strength is known as sarcopenia.[12] Sarcopenia represents an aspect of physical frailty, a component of the greater frailty syndrome, and plays an important role in the development of frailty.[13] It is regarded as the "biological substrate of frailty" since muscle is crucial for physical functioning and for mobilization of amino acids in times of stress response and healing.[13-16]

How is Frailty Measured?

Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a progressive and generalized loss of skeletal muscle and muscle strength.[17] Diagnosis of sarcopenia requires documentation of low muscle mass and either low muscle strength or low physical performance. Existing frailty tools focus on muscle strength and performance but lack a direct measure of muscle mass.

Muscle strength can be easily measured with a handgrip strength test, using a dynamometer to measure grip strength.[18] This simple test correlates with leg strength, is easily measured, and is influenced by age, gender and body mass index (BMI). Physical performance can be ascertained with the Short Physical Performance Battery (SPPB) test, consisting of a gait speed test, time to rise and to sit from a seated position five times without using arms (chair rise test), and ability to balance standing for 10 seconds in a tandem or semi-tandem position, each scored out of 4 for a total score out of 12.[19]

Weight loss is often used to indirectly represent the muscle mass state. However, this measure is flawed because excess adiposity can mask low muscle mass.[20] "Sarcopenic obesity," defined as loss of muscle mass and increase in fat mass, is especially prevalent in the elderly. For example, in a study of elderly cancer patients, while only 7.5% of patients were found to be underweight, almost 50% were sarcopenic when evaluated by a computed tomography (CT) scan.[21]

Muscle mass is an attractive measure of frailty because it is quantitative and independent of patient compliance, acuity, and symptom status, all three of which can vary day-to-day in elderly hospitalized patients. The gold standards for measuring muscle mass are magnetic resonance imaging (MRI) and CT scan.[17] However, high cost and limited access preclude their routine clinical use. Therefore, the preferred method to measure muscle mass for clinical and research use is with dual-energy X-ray absorptiometry (DXA) scan. DXA is a whole-body x-ray scan used to measure body composition aspects such as bone density, body fat, and muscle mass.[22] One of the emerging ways muscle mass can be measured is with bioimpedance.[17,21] The bioimpedance scale uses undetectable micro-currents to measure weight, body fat and muscle mass. It can be located at the point of care and newer technology has vastly improved accuracy.

Artist: *Anais Di Via Ioschpe*

Although there are several frailty scales prominent in the literature, the lack of consensus around which scale to use and the definition of frailty has limited its integration into routine clinical practice and pre-surgical assessment. These scales include the previously mentioned SPPB, the Fried scale, and the Rockwood Clinical Frailty Scale (CFS). The SPPB scale is out of 12, with a score of 5/12 or below needed to diagnose frailty. The Fried scale consists of 5 items, with a score of 3/5 required to diagnose frailty: 5-meter gait speed, handgrip strength, unintentional weight loss, low physical activity, and exhaustion.[6] The Rockwood Clinical Frailty Scale allows for the global assessment of the patient's symptoms, physical activity, energy, mobility, and disability for basic and instrumental activities of daily living, assigned a score ranging from 1 (least) to 9 (most) frail, among others.[23]

Why is Frailty Important?

What is the importance of frailty to everyday clinical medicine? The presence of frailty can indicate a patient's resilience to withstand a stressor. Frail patients are more vulnerable to adverse events and important medical complications. The presence of the frailty syndrome plays an important role in guiding clinical decisions for older adults, as predicting risk is more complex given their highly variable status. Clinicians are able to use the frailty assessment to better predict the risk of adverse events in this population and to choose an appropriate therapy. For instance, a preoperative presence of frailty can indicate the patient's ability to withstand the stressor of surgery, and their postoperative risk of mortality and complications.[2]

In short, the "one size fits all" concept of medicine is gradually being replaced by strategies aimed at delivering personalized medicine to patients. The shift to more individualized care has the potential to improve outcomes, minimize adverse events and optimize patient care. As the world's population ages and the number of older adults is projected to increase dramatically over the next two decades,[24] the population of older adults with frailty and comorbid conditions will increase. It will become increasingly important for future physicians to know how to properly care for these complex patients. Using frailty measures to help guide clinical decisions will become more commonplace and allow physicians to avert unwanted side effects and improve quality of life, underscoring the importance of shared decision making and discussing all risk and benefits with our patients.

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The Triage System Implemented in Israeli Emergency Departments: A Review

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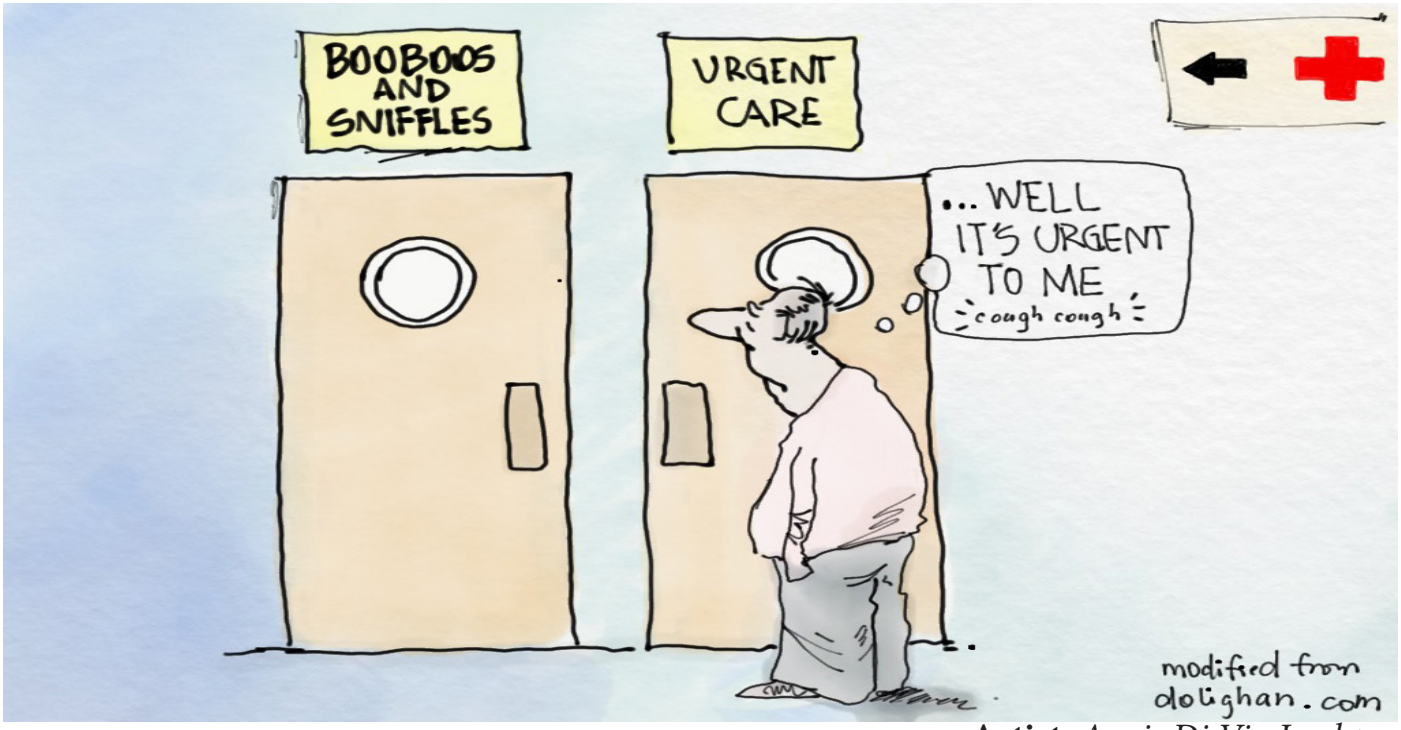

Artist: *Anais Di Via Ioschpe*

Overcrowding of emergency departments is a crucial problem facing hospitals in Israel. According to data from the Israel Health Ministry, occupancy in Israeli emergency departments (EDs) has increased 105% over the past decade. Moreover, two of Israel's hospitals have exceeded their occupancies by 200%.[1] The myriad of issues associated with overcrowding include prolonged waiting times, increased patient morbidity and most notably, increased patient mortality. To combat these unfavorable outcomes, hospitals can classify patients based on severity and urgency (from mild to life-threatening) and allocate hospital medical staff and resources accordingly.

The competent classification of patients based on their conditions can significantly impact patient mortality; correctly identifying high-urgency patients minimizes the time spent diagnosing and treating these patients, thus improving patient outcomes.[2] In addition, correctly identifying low urgency patients can reduce waiting times for patients requiring immediate care, and can help ensure that hospitals use their finite resources appropriately. It is therefore imperative that hospitals employ an established system to proficiently triage patients to maximize patient outcome.

The Canadian Triage and Acuity Scale (CTAS) is one of the established scales used by Israeli hospitals to effectively triage patients in the setting of crowded EDs. It was developed to establish a national standard for triage that emphasizes reliability, validity and improved patient care, by codifying patients into five different levels based on the severity of their illness. The system's levels are as follows: non-urgent (level 5), less urgent (level 4), urgent (level 3), emergent (level 2), and resuscitation (level 1)[3]. For example, presenting-complaints that would be classified as level 5 include sore throat, diarrhea, minor bites and minor contusions, whereas level 1 presenting-complaints include cardiac arrest, unconsciousness, chemical burn ≥25% body surface area, and respiratory arrest. When patients arrive in the ED, most can be assigned a level based on their presentation, chief presenting complaint, history, and vitals[4].

Since its introduction in 1999, the CTAS has undergone extensive evaluation to determine its reliability and effectiveness. A 2015 meta-analysis of 14 studies concluded that the CTAS showed an acceptable level of overall reliability.[5] The universal acceptance of the CTAS has prompted multiple countries, including Israel, to investigate the validity and reliability of the CTAS in their own hospital systems. The Israeli Ministry of health issued national guidelines in 2015 demanding that pediatric EDs use this five-level triage system, and effectiveness has been evaluated following implementation across hospitals. In 2018, the Department of Pediatric Emergency at the Technion-Israel Institute of Technology reported that the pediatric use of CTAS demonstrated validity in a children's tertiary hospital in Israel[6]. This article, published in the European Journal of Emergency Medicine, was notably the first to report on the performance of a triage tool in an Israeli ED.[6]

The CTAS is implemented worldwide to appropriately triage patients according to their need, and previous research has demonstrated a reasonable validity. While it has proven to be effective in specific hospitals, there are concerns over the variability of the system's performance. In Israel, only limited research has been carried out in hospitals since the implementation of the CTAS. Researchers in Israel should pursue further investigation, including evaluation of factors that influence triage system performance, and areas of potential improvement. Efficient and considerate handling of EDs is one essential way that hospitals can continue to improve patient care.

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A Step Beyond the Limits of Medicine

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There is a mysterious landmark in the field of medicine; the invisible line we read in our textbooks or hear through our mentors. As students, we do not run up against the line. We are unable to fully understand the weight of responsibility that a practicing physician feels when they encounter this obstacle. Yet, every time I interview a patient who is homeless, has a terminal illness, or isn't able to afford treatment, I can feel the presence of that invisible line which marks the boundaries of what the field of medicine is able to do.

As students, we like to stay within the boundaries of medicine and rarely do we venture beyond, into the territory of social issues. While it may be easy for us to feel as if these issues are out of our scope of care, in reality they directly affect our daily clinical decisions. As a student volunteer at a refugee clinic looking down at the last two boxes of Amlodipine, I have had to ask myself, "How am I going to split these between the six patients I have to see today?" In the hospital, I remember seeing the same patient every single day for over a month and wondering to myself, "What are we going to do for this patient whom we can't treat anymore but who has nowhere else to go?"

Looking forward, as we mature from students to physicians, we will find ourselves more often making decisions take into account social issues and circumstances of our patients. In deciding whether to discharge a patient, we have to be aware that patients with poor socioeconomic circumstances may require extra consideration, as their care may be interrupted when transitioned from a hospital to a home setting. Patients who have poor health literacy or are poorly motivated may require different treatment regiments or more frequent follow up appointments.

Not only must physicians make decisions informed by our patients' social circumstances, we may have to step beyond the realm of medicine to tackle the issues themselves. In pediatrics,

Artist: *Lital Avni-Singer*

I met a 6-month old boy who had lost most of his brain to severe hydrocephalus, but had parents with significant intellectual disability, who weren't willing to let go. The child couldn't even breathe for himself, but he was all these parents had. What can we do in such a situation? The doctors did not try to miraculously save him, because there was no saving to be done. Instead, they tried to minimize the family's pain and were present to guide and comfort the grief-stricken parents. Eventually, their son was allowed to pass.

To be a physician is not always to be a hero. We, as students and physicians, all practice, study, and prepare, day after day, year after year, so that we can know all that there is to know, and so that we can do all that can be done for our patients. And yet, even having prepared to the utmost, when the next patient arrives, you could find yourself with no guidelines and no textbook answer to meet your patients' needs. You don't know what to do, because ultimately, no one can know what to do. To be a physician is not to be a hero; when you encounter the limits of what medicine can do, have the courage to step beyond.

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Preliminary Analysis of Predictors of Follow-up Likelihood in Israeli CHD Pediatric Patients

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Background

Congenital Heart Disease (CHD) is the most common congenital anomaly worldwide, with a live birth rate of 9 per 1000 live births (4). Due to advances in modern medicine, babies born with CHDs have a greater than 85% survival into adulthood. Such a high rate presumes lifelong cardiac care for the majority of patients, as well as specialist cardiac care for over half of adult CHD patients (6). Most patients presenting with isolated and less complex defects have a normal life-expectancy. Conversely, patients presenting with more complex CHD variants exhibit mortality rates between two to seven times higher than the general population (5). These patients may suffer severe complications, including heart failure, endocarditis, arrhythmias, and pulmonary hypertension. Preventing, monitoring and treating such sequelae emphasize the importance of appropriate follow-up care (5).

Despite the clear need for ongoing medical attention within this population, many adolescent CHD patients are lost to follow-up as their care is transitioned from pediatrics to adult cardiology. This phenomenon of failing to appropriately transition adolescent care has been noted in several countries with disparate rates of treatment-disengagement. Canadian researchers showed a high proportion of patients lost to follow-up; defined as patients with complex CHD over 18 years who did not receive cardiac care subsequent to their graduation from pediatrics. This group constituted nearly 27% of those surveyed (8). In Belgium, however, the number of CHD patients lost to follow-up following this transition was reported at only 7.3% (3). This is in contrast to an American study that found a rate as high as 76% (3, 7). These fluctuations in data may be attributed to disparate definitions of "loss to follow-up" within studies, underlining the need for an international, multicenter study utilizing standard definitions (4).

Despite a 2012 survey reported the prevalence of CHD in Israel as 5.6 per 1,000 live births, there has yet to see publication of a comprehensive study considering follow-up rates of pediatric CHD patients within Israel (2). As such, we decided to conduct a cohort study of 414 CHD patients treated within Schneider Children's Medical Center, which serves approximately 70% of Israeli children born with CHD (1). We focused on predicting follow-up likelihood between categorizations including: gender; age; clinic visits; diagnostic severity; catheterization-procedures required; surgical-interventions necessitated; and number of diagnosed defects. We hypothesized that follow-up utilization would positively correlate with scores across categories excluding gender and age.

Methods

In 2015, data was collected from CHD patients within a patient databank at Schneider's Children's Hospital in Israel. A standard logistic regression was used to analyze the data via STATA.. The primary variable we evaluated was whether a patient would follow-up at an adult clinic.

Results and Discussion

The studied cohort consists of 414 participants, of which 52% of participants were male. The average participant age was 24 years old, and the average number of hospital visits was 12. Considering level of diagnostic severity, the sample seemed skewed towards more severe diagnoses, with a mean level of severity

of 1.9, and a range of 1-3 (defined as 1 being the least severe, 3 being the most severe) (Table 2).

Additionally, our patient sample showed a wide spectrum of cardiac abnormalities (Table 3). The most commonly found cardiac abnormalities observed in the sample were aortic abnormalities and congenital defects. Within the category of aortic abnormalities, the prevalent diagnosis was aortic regurgitation, and the most common congenital defect surveyed was ventricular septal defect (VSD). As was expected, most patients in this sample had been diagnosed with 1-2 heart conditions (table 4).

We performed a logistic regression on the patient data shown in Table 1 testing variable-influence on the likelihood of patient follow-up. We posited the following variables to be positively-predictive of follow-up: level of severity; number of surgeries; and number of catheters. This was based on the assumption that increased severity necessitates treatment, therefore motivating follow-up.

However, we were surprised to find the logistic level of both severity and number of catheterizations to be statistically-significant negative-predictors of patient follow-up. Examining correlation coefficients between level of severity, number of surgery variables,' and number of catheters variable also revealed negative correlation coefficients (Tables 1 & 4).

Additionally, age at diagnosis and number of visits were positively-predictive for likelihood of follow-up (Table 1). Intuitively, we thought the more previous visits should lead to increased willingness to pursue and continue treatment due to our presumption that number of previous visits would be indicative of disease severity. However, our dataset does not include patient survival which may present a confounding variable. Furthermore, extrapolating could potentially explain the negative relationship between likelihood of follow-up, number of catheterizations, and disease- severity, assuming a positive-relationship between patient-mortality and level of disease burden. Additionally, this could also explain the negative correlation between level of severity, number of surgeries, and number of catheterizations. If a patient does not survive long enough to receive said interventions, the aforementioned relationship now makes greater intuitive sense.

Given the breadth and depth of our dataset, we believe that continued analysis should be carried out with the hope of further elucidating the factors influential for patient follow-up in this specific population. There are a number of different ways this analysis could proceed: firstly, looking at how different types of diagnosis affected the likelihood of follow-up. Such an analysis can be done via statistical techniques we used for this study; however, the amount of data-coding required is considerable. Yet, doing so would provide explanatory power as to how specific heart conditions, rather than level of severity, related to different types of heart conditions and increased or decreased the likelihood of follow-up.

Secondly, the data used in this analysis was collected in 2015 without including patient mortality. Including this data may help clarify some anomalies in

Artist: *Olivia Keller-Baruch*

our analysis. Furthermore, this data should not be difficult to collect, as it could be gathered by accessing the original hospital-database. We believe that this variable will make a major contribution to our dataset and constitutes a logical sequence for study-continuation. We are currently collating a more updated version of our dataset in order to help further explore the relationship between CHD diagnosis and patient follow-up.

Finally, more advanced statistical techniques could be used in order to further control for variables such as: length of time between final child-clinic visit and initial adult clinic visit; distance between original medical center and follow-up medical center; and whether the year of diagnosis affects likelihood of follow-up. These techniques could also be employed in the follow-up study which will include patient mortality data.

In conclusion, our analysis showed a multiple significant predictor of likelihood of follow-up after diagnosis with a heart condition (Table 1). Specifically: age at the time of diagnosis, and number of previous visits, were positive predictors of patient follow-up. Surprisingly, the level of diagnostic-severity and number of catheterizations negatively predicted follow-up. We believe this may be due to an underlying confounding variable within our dataset— patient mortality status. The conclusions of this study underscore the need for additional data and analysis to fully understand the relationship between these variables.

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COMMENTARY/REVIEW

Investing in quality-of-life treatments vs. life-saving treatments as observed through dermatological pathologies

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Clinical trials are essential to quantify how novel treatments or therapies for specific pathologies affect patients. At their core, such trials are both financially and ethically motivated; they represent the forefront of medicine and attempts to cure diseases, and yet they need to generate enough money to support one of the world's largest industries. Defining the population who may benefit from a novel therapy is also replete with contradictions. In the following discussion, we aim to review how new treatment initiatives are planned, utilizing an observed case of drug-induced pemphigus foliaceus (PF) for discussion.

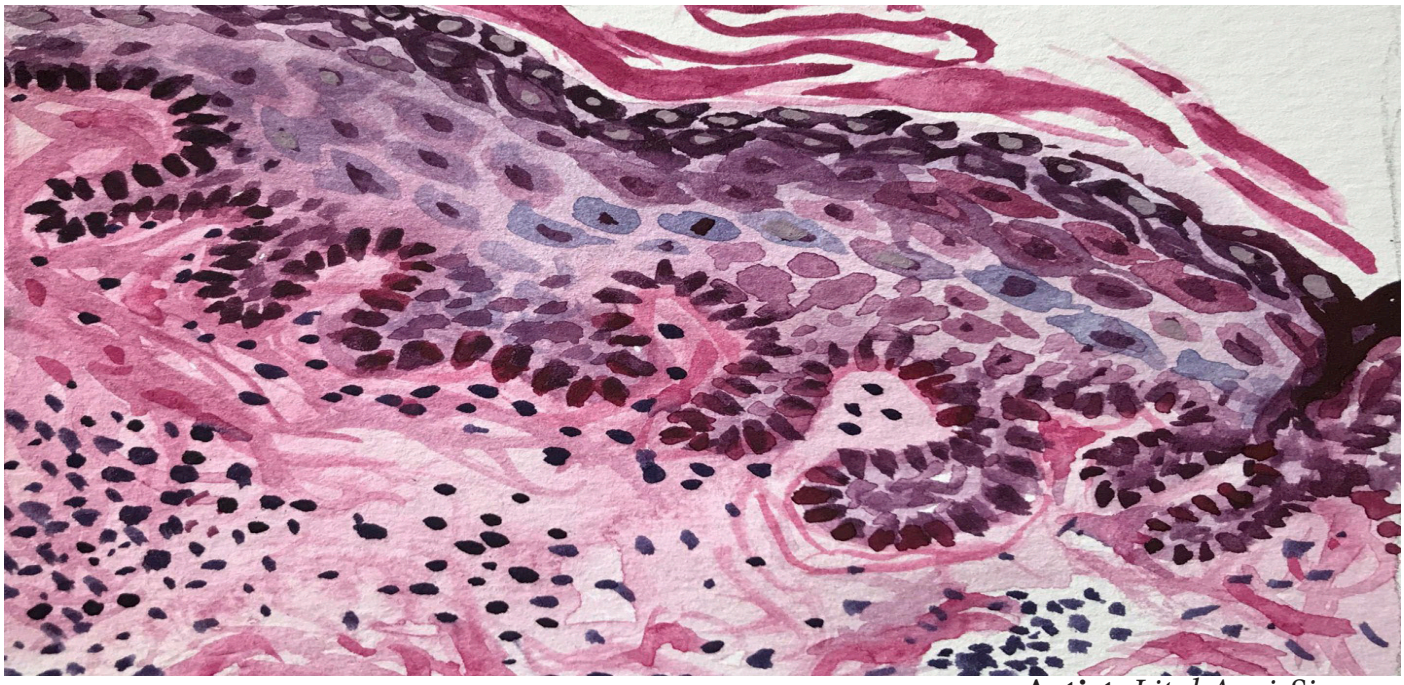
When the body's defense system malfunctions, inappropriate responses are generated against self-antigens.[1] If these self-antigens are of dermatological origin, the diseased states can manifest as connective tissue diseases and immunobullous diseases .[2] Pemphigus represents a family of destructive blistering conditions, characterized by disruption of intracellular adhesions causing epithelial and mucosal blistering.[3] This autoimmune dermatological disorder has multiple subtypes with varying severities. The severity of each condition is not clearly defined as some subtypes are fatal while others result in devastating chronic illness. Some subtypes of pemphigus involve the mucosal membranes which can result in direct, life-threatening conditions, due to interference with pulmonary and gastrointestinal membranes.

Another subtype is PF, which affects only the skin and spares mucosal membranes, and includes subcorneal acantholytic blisters.[4] PF most commonly affects the scalp, face, and trunk, and in most cases originates in superficial blisters that develop into scaly, crusted epithelial erosions. . As the disease progresses, lesions may remain localized to a single area of the body, but may also spread to cover larger areas.[5] Presently, the etiology of PF is not fully-understood, beyond being considered an autoimmune condition. Risk factors for PF are stated clearly in the literature[2,3,4]; The field assumes that intrinsic (genetic) and extrinsic (environmental) factors interact and play roles of unknown magnitude in the pathogenesis of pemphigoid diseases.

Treatment and management of these disorders is complicated and usually involves management of the immune system, along with other co-existing pathologies which may be secondary to widespread infection-susceptible blistering. When cases are environmentally-triggered or drug induced, the instigator should be identified and removed from contact with the patient. Current gold-standard medical intervention for dermatological autoimmune disorders includes a combination of corticosteroids and steroid-sparing immunosuppressants.[5]

PF has no cure,[6] is not directly fatal, and its symptoms are less directly life-threatening than other pemphigus subtypes. However, it may lead to a severely reduced quality of life due to the inability to carry out simple tasks and the significant psychological toll on patients.[7]

The observed case that prompted this reflection was a complicated one; multiple systemic inflammatory insults made therapeutic management highly complex. Expert dermatologic consultation enabled adherence to professional guidelines, with concurrent inpatient hospitalization involving a long-term immunosuppressant regimen throughout. Over time, the immunosuppressive regimen improved the patient's presenting skin condition. However, the weakened immune system and open wounds left the patient susceptible to multiple complications including: acute kidney injury; multidrug resistant bacteremia; fungemia; and bacterial



Artist: *Lital Avni-Singer*

sepsis. Such complications arising from open skin blisters require aggressive wound care, as systemic infections may prove fatal.

PF is very rare condition in the United States (US) and presents more commonly in regions of South America and North Africa.[8] As there is no acute, direct threat to life from PF, treatments are scarce. Rather, therapeutic management focuses on containing PF and treating secondary infections. The autoimmune nature of the condition makes immunosuppressive therapy the treatment of choice, but these medications also confer increased of susceptibility to multiple secondary systemic infections, which can be life-threatening. The combination of low direct mortality-rate and low prevalence in the developed world leads to little innovation in the search for a cure. As of writing this reflection, only four clinical trials are testing novel drug therapies, one of which is outside of the US. These nascent targeted therapies include: manipulation of native regulatory T cells to make chronic immunosuppressive therapy obsolete; disruption of B cell receptor signaling; and neonatal Fc receptor inhibition.[9]

More therapies are being developed for the lethal subtypes of pemphigus. While developing novel treatments for lethal conditions is crucial to advance healthcare, chronic conditions are also important to treat. Chronic dermatologic pathologies, as described above, are unlike other chronic illnesses because they cannot be effectively managed without putting the body at great risk, due to constant blistering and painful external wounds. The purely superficial presentation of PF, while lacking direct fatal complications, still renders patients at risk for painful, open blisters and subsequent wounds that are susceptible to dangerous secondary infections. It should be noted that more treatment opportunities exist for these conditions outside of the US, particularly in Europe where extracorporeal immunoadsorption is performed to remove auto-antibodies from the blood.[10] In the US, this treatment is not available for this type of dermatological autoimmune condition. Patients suffering from chronic, autoimmune dermatologic pathologies need more effective treatment methods, without the risks associated with immunosuppression. Developing new treatments and implementing effective disease-management techniques are crucial for more efficient management of the condition and in order to improve physical and psychological quality of life.

Fatal diseases that endanger multiple populations across the world must be treated, researched, and considered promptly. Unfortunately, patients suffering with severe conditions that greatly reduce quality of life, and yet are not life-threatening, have few prospects for life-changing treatment innovations. The patient in the case presented above was told that their condition has no curative possibilities or prospects, and that there are no current studies underway. The medical community owes such patients more attention, and owes more consideration to non-life-threating conditions.

List of abbreviations

PF: Pemphigus Foliaceous
IVIG: Intravenous Immunoglobulin
US: United States

Authors' contributions

TL observed the discussed case. IH reviewed and developed the discussion. Both authors reviewed and edited the reflection.

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Medicine is a Team Sport

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I currently work in vaccine hesitancy and infectious disease, but I started my medical journey working with a neurosurgeon.

On Monday mornings, I would start the week with the Brain Tumor Board meeting: 50 surgeons and other physicians, physicians' assistants, nurses, techs, and students gathered to discuss the coming week. This was conducted as a learning exercise wherein senior surgeons quizzed the younger doctors, and was a place to ask for help and advice from peers, relying on others' expertise. For a tough case, the more thought, the better. My mentor tells his patients that they are getting a free second, third, and fourth opinion.

My mentor is one of the top neurosurgeons in the country. If I had a brain tumor, I would trust him with my life. However, he is not an endocrinologist. So, when the group was discussing a patient with acromegaly, he asked an endocrinologist for advice. It's not his field – and he knows it. But he's aware that he has a world-class team right in the dugout with him.

Medicine is a team sport; nobody is expected to know every answer.

When I'm talking to vaccine-hesitant parents, they often express distrust in their children's doctors, because they cannot recite every ingredient (or, technically, excipient) in a vaccine, nor explain the reason why each of those ingredients is used. These parents seem to think that doctors ought to possess an encyclopedic knowledge of medicine, and they lose trust when they don't know everything. This erosion of trust makes them less likely to vaccinate their children, thereby damaging the community immunity we rely on to keep us free from vaccine-preventable diseases like measles, flu, and diphtheria.

Medicine is not a solo show; we are reliant on our colleagues to augment our knowledge because it would be impossible to know everything. A pediatrician may not know the formula for a vaccine, nor the reason why polysorbate 80 is involved. But we need to trust that they're getting her data about safe levels of polysorbate 80 from someone who does know. A doctor may not be able to explain how aluminum hydroxide, a commonly used adjuvant, interacts with the blood brain barrier. Even so, it's a near guarantee that they base her professional decisions off of the work of scientists who have spent their careers asking and answering that very question.

To those on the outside, medicine is an esoteric field. Most patients don't understand what really goes on behind the scenes. I understand that parents fear long lists of ingredients and excipients within the vaccine, especially if some provoke negative associations. For example, what is formaldehyde to the lay person?

Artist: *Niko Morozov*

Embalming fluid! However, it's also produced in the body and present in vaccines in miniscule amounts. The dose makes the poison.

As a medical community, we need to be honest about what we know and what we don't know. But that is not enough—we also need to be transparent about our decision-making. Telling a parent to just do the thing and then shooing her away won't create a trusting relationship; in fact, it often creates the opposite. Many parents whom I've spoken to have such little faith in the medical establishment that they take their concerns to alternative practitioners, who may confirm these parents' biases through recitation of anti-vaccine rhetoric, amongst other harmful ideas.

So why don't we tell parents and patients, "You know what? I don't know the answer to your question, but I can direct you to some literature published by experts in the field who have studied this and have determined that it's safe to use, and I'm here to answer any questions I can?" This approach may help.

There is a rumor that doctors receive only half an hour of vaccine education whilst in medical school. We don't have a formal class about vaccines—in the grand scheme of things, they're not worth the time. We know that vaccines are safe and effective, and therefore it would be imprudent to study their production-pharmacology; that is for our colleagues in pharmacology school. We still have hours upon hours of chemistry classes, immunology, and physiology… all of which enable us to understand the way that vaccines work in our bodies.

When parents and patients worry about the amount of vaccine education received, we need to be honest with them: we do not learn how to produce a vaccine, and most of us cannot recite what their ingredients, besides some basic facts (Is it live-attenuated? Inactivated? Conjugate?). However, as a medical community, we work with people whose lives are spent on such questions—and we trust them.

Like it or not—this presents a barrier preventing many from trusting doctors, and we need to reconsider the way we approach dialogue with skeptical patients. It's on us to remind those who are hesitant that we're not playing alone; we have experts around the world as teammates.

An Introduction to Artificial Intelligence and its use in Pancreatic Cancer Diagnostic and Treatment

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As artificial intelligence (AI) continues to blossom in the world of medical research, it is becoming increasingly necessary for medical students and faculty alike to have a basic understanding of artificial intelligence and how it can be applied for research purposes [1]. With more scientific literature utilizing AI, its effectiveness as a research tool is also becoming more apparent [1] [2]. The goal of this article is to provide a brief introduction to AI, deep learning, and how it can be applied to diagnosing pancreatic cancer.

Artificial intelligence is commonly described as being similar to the human brain in the sense that there are a series of interconnected nodes which are able to communicate with each other in order to analyze data, similar to a network of neurons and synapses [1] [2]. Machine learning can be categorized into two types of learning: supervised and unsupervised. In supervised learning, the AI network is trained using already labeled data. Put into other terms, the machine has some degree of guidance as it learns from the dataset because there are predefined input-output pairs. In contrast to supervised learning, unsupervised learning does not use data with predefined input-output pairs.

There are advantages and disadvantages to both of these techniques. While unsupervised learning is a much more powerful analysis tool, it suffers from the fact that it is generating de novo relationships in the data and there is no telling what relationships it might decide to weigh more heavily than others. In addition, unsupervised analysis also requires a great deal more computing power and data to generate a fully functioning neural network. In contrast, supervised learning can generate a neural network using less data, but is restricted by the quality of the input-output pairs that it is trained on.

Once generated, a neural network is composed of layers of nodes. These nodes can be thought of as the neurons of the system, and the nodes of different layers communicate with each other in order to form the neural network. In most basic terms, there are three types of layers: the input layer, the output layer, and the hidden layers. The hidden layer connects the input and output layers through a series of different pathways between nodes. There can be any number of hidden layers between the input and output layers depending on the complexity of the neural network. The more data and the higher quality it is, the more fine-tuned the neural network will be.

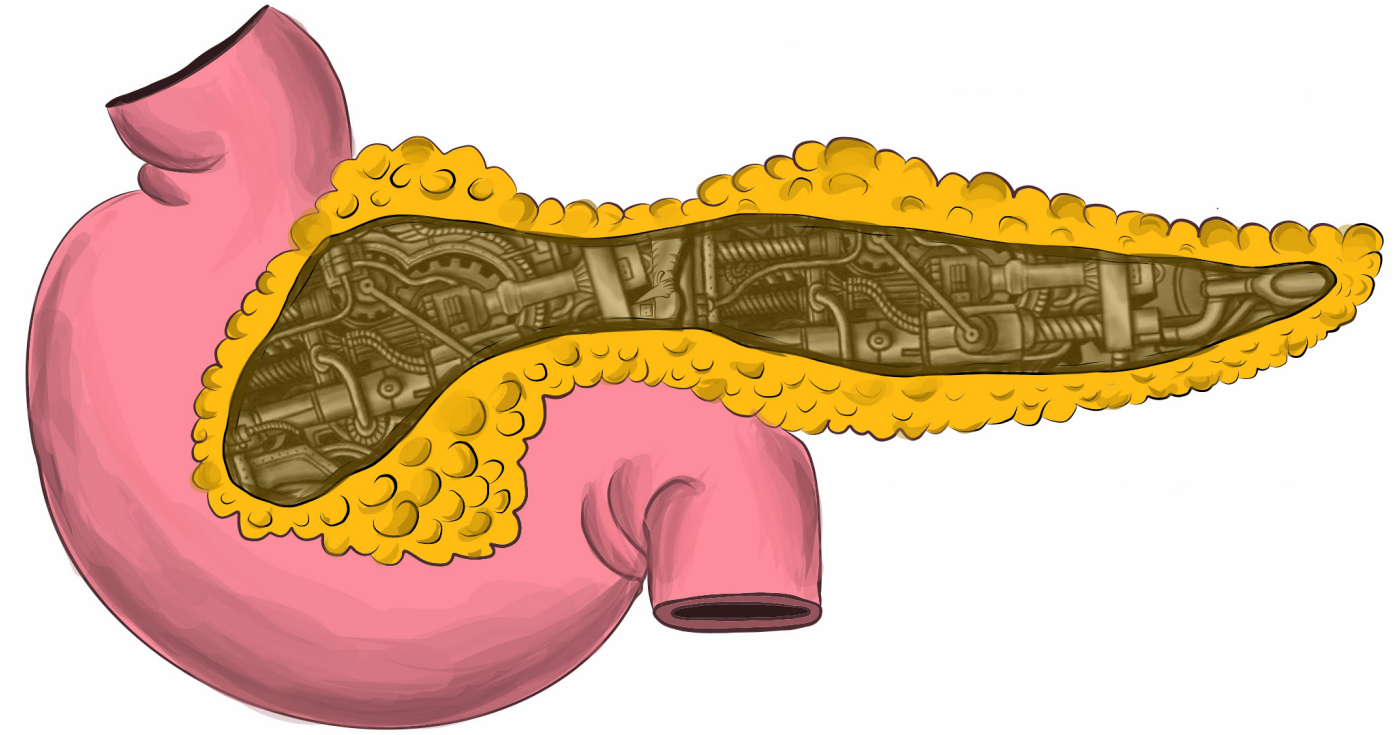
While incredibly powerful, the use of AI is still not without its constraints. Mainly, the neural network is highly dependent on the quality and quantity of the data available. Without large amounts of training data (when using supervised learning), it is difficult to generate an effective neural network. In addition, there is a deeper issue of not entirely understanding how neural networks are able to generate connections between nodes and data points.[6]. However, the use of AI is growing at an astonishing rate; more data is being analyzed to generate new sets of relationships, improve diagnostic techniques, and capture video and picture analysis to aid physicians in real time during procedures [7][8][9].

Pancreatic cancer is considered one of the most difficult cancers to both diagnose and treat due to its variation in size and shape, and because of its

anatomic location. These challenges contribute to the reason why pancreatic cancer is the fourth leading cause of cancer-related deaths in the United States and why it is usually diagnosed very late in its course [3]. Furthermore, due to diagnostic difficulties and available diagnostic options, the 2-year survival is only about 10% after being diagnosed with metastatic pancreatic cancer [4]. Diagnostic radiologists still have trouble diagnosing pancreatic cancer and errors are fairly common; a study in 2014 showed that the preoperative diagnosis accuracy of pancreatic neoplasms was only 61% [5]. Extensive research and development have been conducted in order to expand the capabilities of diagnostic radiology to better diagnose pancreatic cancer at an earlier stage, through the integration of artificial intelligence. This emphasis on interweaving new technology into radiology has created the field of radiomics, the analysis of large amounts of imaging data to help develop better diagnostic models [6]. Through the new modalities of radiomics and artificial intelligence, radiologists have started developing new models and algorithms to better predict, diagnose, and treat pancreatic cancer.

There have been a number of novel applications with regards to AI in the treatment and diagnosis of pancreatic cancer. For example, the Wisense System, a real time deep learning system to monitor blind spots during esophagogastroduodenoscopy was shown to reduce the number of blindspots in a randomized control study [5]. In another recent study, AI was trained on pancreatic fine needle aspiration cytology slides and was able to distinguish between benign and malignant cells with the same level of accuracy as trained cytopathologists. A more novel approach to the use of AI in pancreatic cancer involves elastographic mapping of pancreatic masses [9]. A common issue when it comes to diagnosing pancreatic cancer is physicians' ability to distinguish between chronic pancreatitis and pancreatic adenocarcinoma from endoscopic ultrasounds. AI was trained using endoscopic ultrasound videos with elastography from patients with chronic pancreatitis or pancreatic adenocarcinoma, and AI was able to diagnose pancreatic cancer and chronic pancreatitis with 87% and 83% accuracy respectively.

Supervised learning models have been particularly effective in helping to provide radiologists with a second opinion on their diagnosis. The integration of a computer learning model that focuses on radiomic signatures, such as region or volume of interest, ultimately helps reduce both inter- and intra-reader variability [10]. In one specific case, a computer aided diagnosis model was created that factored in 22 variables: 5 guideline-based variables and 17 radiomic variables. The guideline variables are traditionally taken into account and recorded by a radiologist



Artist: *Olivia Keller-Baruch*

such as cyst size, location, shape, and sex of the patient [11]. On the other hand, the radiomic variables are data that was obtained from CT scan imaging analysis, such as intensity and texture analysis of the neoplasm. The data showed that the accuracy of the 5 guideline features was only 70%, but after integrating the 5 guideline variables with the 17 radiomic variables through a support vector model (SVM) model, the accuracy increased to 77% [11].

Currently, there are also investigations on pancreatic cancer markers using AI, specifically trying to differentiate between benign and cystic pancreatic lesions by analyzing cyst fluid. In a 2019 study, AI was trained to differentiate between benign and cystic lesions using carcinoembryonic antigen, carbohydrate antigen 19-9, carbohydrate antigen 125, cyst fluid amylase, sex, cyst location, connection of the pancreatic duct and cyst, type of cyst, and cytology predictive factors [12]. While this study showed that AI was able to improve the diagnostic potential of cyst fluid analysis, its conclusions were severely held back by the lack of data available for the study.

We hope that this brief summary of artificial intelligence and some of its uses can help provide some clarity with regards to how AI is being currently used in medicine. In summary, AI has been shown to hold great potential in the field of diagnostics and treatment of pancreatic cancer. It is proving to be useful in areas previously constrained by current diagnostic and treatment techniques. There are a number of ways that AI is being used to improve patient outcomes and to aid physicians in real time. Based on the current literature, AI has the potential to push the boundaries of medicine and improve patient outcomes.

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