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ORIGINAL RESEARCH

Identify and monitor clinical variation using machine intelligence: a pilot in colorectal surgery

Kamal Maheshwari[1,2] · Jacek Cywinski[1] · Piyush Mathur[1] · Kenneth C. Cummings III[1] · Rafi Avitsian[1] · Timothy Crone[3] · David Liska[4] · Francis X. Campion[5] · Kurt Ruetzler[1,2] · Andrea Kurz[1,2]

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Abstract

Standardized clinical pathways are useful tool to reduce variation in clinical management and may improve quality of care. However the evidence supporting a specific clinical pathway for a patient or patient population is often imperfect limiting adoption and efficacy of clinical pathway. Machine intelligence can potentially identify clinical variation and may provide useful insights to create and optimize clinical pathways. In this quality improvement project we analyzed the inpatient care of 1786 patients undergoing colorectal surgery from 2015 to 2016 across multiple Ohio hospitals in the Cleveland Clinic System. Data from four information subsystems was loaded in the Clinical Variation Management (CVM) application (Ayasdi, Inc., Menlo Park, CA). The CVM application uses machine intelligence and topological data analysis methods to identify groups of similar patients based on the treatment received. We defined "favorable performance" as groups with lower direct variable cost, lower length of stay, and lower 30-day readmissions. The software auto-generated 9 distinct groups of patients based on similarity analysis. Overall, favorable performance was seen with ketorolac use, lower intra-operative fluid use (< 2000 cc) and surgery for cancer. Multiple sub-groups were easily created and analyzed. Adherence reporting tools were easy to use enabling almost real time monitoring. Machine intelligence provided useful insights to create and monitor care pathways with several advantages over traditional analytic approaches including: (1) analysis across disparate data sets, (2) unsupervised discovery, (3) speed and auto-generation of clinical pathways, (4) ease of use by team members, and (5) adherence reporting.

Keywords Machine intelligence · Clinical monitoring · Clinical pathway

1 Introduction

According to the Institute of Medicine, minimizing unnecessary practice variation is vital to provide high quality healthcare [1]. High quality healthcare should be safe, effective, patient-centered, timely, efficient and equitable. Care pathways help achieve the goal of high quality healthcare by providing safe and effective interventions more consistently. The worldwide scientific community has embraced standardized clinical pathways as a useful tool to reduce variation in clinical practice [2]. Enhanced Recovery after Surgery (ERAS) programs are standardized clinical pathways that are gaining widespread acceptance to reduce postoperative morbidity and improve perioperative outcomes [3, 4]. However, adherence to these clinical pathways is often poor due to a lack of good evidence supporting the benefit of individual components of the ERAS pathway. Also, monitoring adherence to clinical pathways is challenging due to the complexity of healthcare data [5, 6]. Lack of evidence stems from the high cost, complexity and time requirement to run clinical trials in the complex healthcare environment. Fortunately, new methods of large scale data analysis utilizes machine intelligence to identify clinical variation and provide actionable insight into clinical practice using near-real

✉ Kamal Maheshwari
maheshk@ccf.org

[1] Department of General Anesthesiology, Anesthesiology Institute, Cleveland Clinic, 9500 Euclid Ave — E31, Cleveland, OH 44195, USA

[2] Departments of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, 9500 Euclid Ave — E31, Cleveland, OH 44195, USA

[3] Department of Hospital Medicine Cleveland Clinic, Cleveland, OH, USA

[4] Departments of Colorectal Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH, USA

[5] Ayasdi, Inc, Menlo Park, CA, USA

time data [7–9]. This unsupervised and unbiased way of learning is a truly data-driven method of identifying patient characteristics and care events associated with both positive and negative patient outcomes thus guiding clinical pathway development.

The goal of this project is to identify variation in clinical practice and outcomes utilizing machine intelligence in colorectal surgery patients. Identifying this variation can help guide creation and optimization of care pathways. We do not, however, intend to provide evidence for a causal relationship between care pathways and outcomes improvement. We report the use of a particular application of machine intelligence called the Clinical Variation Management (CVM) platform (Ayasdi, Menlo Park, CA) to identify practice patterns in colorectal surgery in the Cleveland Clinic hospital network. The software is specifically designed for discovering clinical variation, automating clinical pathway development and monitoring physician adherence to already described best practices.

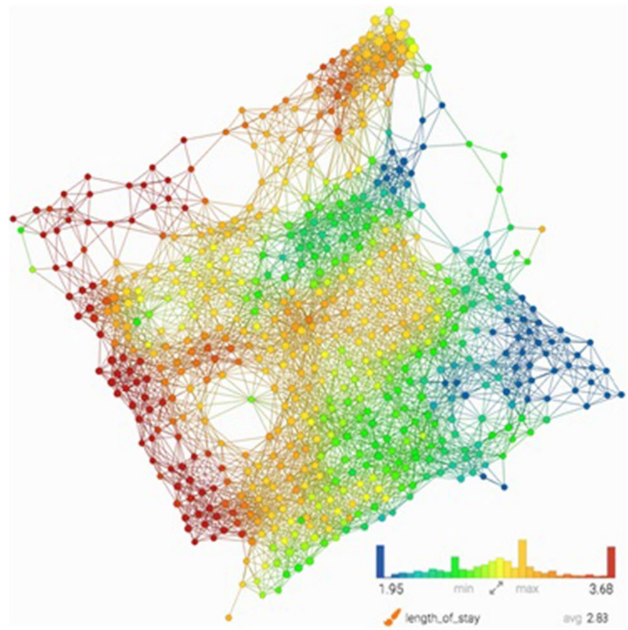

Fig. 1 Topographical data analysis. Each node in this topology represents a group of patients with similar LOS. Blue color represents the lowest LOS, red color represents highest LOS and rest in between. *LOS* length of stay

2 Methods

This collaborative effort started after approval from the institutional clinical and management teams in the Anesthesiology Institute, Digestive Disease and Surgery Institute, and the Enterprise Business Intelligence group at Cleveland Clinic and received a waiver of consent from the Cleveland Clinic Institutional Review Board.

Data from 1786 patients undergoing colorectal surgery from 2015 to 2016 across nine Ohio hospitals in the Cleveland Clinic System was loaded in the CVM application. The CVM is a machine intelligence application focused on rapid unsupervised analysis and insight development from multidimensional data sets. Primarily, the application uses topographical data analysis [10] which helps (1) precisely segment large data sets, (2) identify the underlying features that drive segmentation, and (3) create effective predictive models [11] (Fig. 1) The source of data included the following four Cleveland Clinic information subsystems:

1) Inpatient Electronic Health Record (EHR) data from Epic Systems (Verona, WI),
2) Medications from the Medication Administration Record,
3) Intraoperative anesthetic details from our electronic anesthesia information system (e.g. anesthesia start time, IV fluid volumes, etc.), and
4) Cost data from the cost accounting system.

Data were assembled using specifications from the HL7 interoperability standard known as FHIR. This allowed for intuitive descriptions of problems, medications, and procedures as well as units and time elements.

We created some “user defined” data elements to investigate specific clinical issues related to anesthesia and surgery. For example, our interest in studying trends in intra-operative intravenous fluid administration led us to pre-calculate crystalloid IV fluid volumes based on 3 groupings (< 2000 cc, 2000–2999 cc, ≥ 3000 cc) before loading the data into Ayasdi CVM.

The CVM application uses machine intelligence to identify groups of similar patients based on the treatment received [10] This enabled rapid analysis of all cases together as well as six specific procedure sub-cohorts (Table 1). We defined “favorable performance” as groups with lower direct variable cost, lower length of stay, and minimal 30-day readmissions.

Machine intelligence enabled high-level evaluation of groups to gain initial insight into the clinical factors and treatment events differentiating less favorably and more favorably performing groups. We examined over 30 specific aspects of care including details of demographics, pre-operative evaluation, perioperative antibiotics, intra-operative fluids, blood use, anesthetic approach, anesthetic agents, surgical instrumentation, surgical supplies, multimodal pain management, anti-emetic regimens, diet type and timing, and patient activity status. Time series analysis of “events” (e.g. medication administration, surgical supplies, diet orders, etc.) were displayed allowing the user to see the

Table 1 Procedure types

Procedure type	Patient count	Procedure codes (CPT)
Open partial colectomy	n = 307	44140, 44143, 44144, 44160
Open total colectomy	n = 222	44150, 44155, 44157, 44158
Lap partial colectomy	n = 468	44204, 44205, 44206
Lap total colectomy	n = 315	44210, 44211, 44212
Open rectal	n = 219	44145, 44156, 45110, 45112, 45119
Lap rectal	n = 209	44207, 44208, 45395, 44397
Other	n = 46	Not specified

CPT current procedural terminology, *Lap* laparoscopic surgery

sequence of treatments received by patients in relation to the surgical start time, our index event. For example, administration of antibiotics within 1 h of surgery, an important component of care pathways, can easily be analyzed. The system generated multiple groups based on similarities and performed group-to-group comparisons. We focused most of our analysis on the open partial and laparoscopic partial colectomy (CPT-defined procedure types) sub-cohorts for purposes of the pilot. All findings were stratified by surgeon performing the procedure and hospital where procedure was done.

2.1 Timeline

We conducted the full project over a 12-week period. This included the time of data loading, syntactic validation and semantic validation which accounted for 10 weeks. (Fig. 2) The final 2 weeks included the analysis and report generation. Actual time of analysis was 10 h.

3 Results

In the "All patients" cohort of 1786 patients, machine intelligence auto-generated 9 distinct groups of patients based on similarity analysis (Fig. 3). The system identified a group of 141 patients that was labeled "Best group" (most favorable outcomes group) by the team due to low mean LOS of 2.94 days, low cost and low 30-day readmission rate of 0.7%. The finding was validated by the increased occurrence of current evidence based interventions in this group. For example, frequent use of ketorolac and the avoidance of fluid overload in the "Best group." The results from four distinct area of investigation are reported below.

3.1 Ketorolac use

Ketorolac is a non-steroidal anti-inflammatory drug. Although beneficial for pain management, it is used consistently in colorectal surgery [12, 13]. We analyzed the

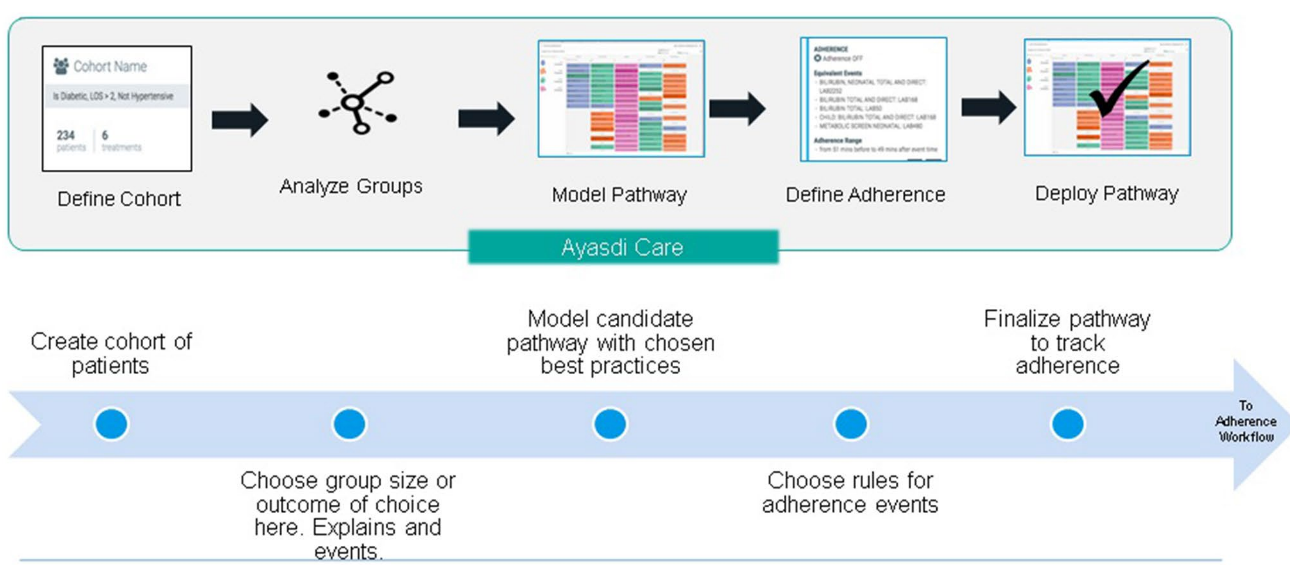

Fig. 2 Pathway workflow

Fig. 3 Autogenerated subgroups. **A** Summary of a subgroup, **B** Each row depicts individual patient care event, **C** Details of patient care event

relationship between ketorolac and outcomes, LOS and direct cost per case. In the "best group" of 141 cases with very favorable performance, low cost, low LOS and few readmissions, ketorolac use was notably higher (n = 77, 54.6%) compared to all colectomy patients (n = 790, 44.2%) but not statistically significantly so (p = 0.071). Qualitatively we could see a difference in the relative timing of ketorolac administration by examining the time series display (Fig. 4).

To further analyze the association between outcomes and ketorolac, we segregated the open partial colectomy sub-cohort into those with and without ketorolac (Table 2). Those receiving ketorolac (n = 99, 32.2%) had lower mean

Fig. 4 Analysis of patient care events for auto-generated laparoscopic surgery group. Each row catalogs all patient care events in a time series. Ketorolac administration is highlighted for each patient

Table 2 Ketorolac detail in open partial colectomy

n = 307	Patient count (%)	LOS	Cost	Diabetics (%)	Hyper-tensive (%)	Read-mission (%)
Open partial with ketorolac	n = 99/32.2	8.35	Low	3.0	14.1	9.1
Open partial without ketorolac	n = 208/67.8	8.87	High	10.3	23.0	8.9

LOS length of stay, *Cost* cost of care for surgical episode

LOS compared to those not receiving ketorolac (n = 208); (8.35 days vs. 8.87 days). Mean cost per case was also lower for those receiving ketorolac compared to those who did not receive ketorolac.

Overall, ketorolac use was associated with lower LOS and cost per case in the "All patients" group and in multiple sub-cohorts. However, absolute differences in ketorolac use rates in the best performing group compared to all others was not statistically significantly different.

3.2 Intra-operative fluids

Nearly all operations require intravenous fluids for drug administration and intravascular volume repletion. Mismanagement of fluid administration—in volume, type, or timing—may cause postoperative complications and worsen survival [14]. It has been demonstrated that the individual provider accounts for the majority of variability in intraoperative fluid administration [15]. We analyzed the relationship between intra-operative fluid volume administered and outcomes (Table 4). We defined crystalloid as the use of lactated Ringer's solution or normal saline. We compared rates of fluid use in the patient groups generated by the using machine intelligence described above and found a strong association with lower intra-operative fluid use (< 2000 cc) in the lower LOS and lower cost groups. We compared the use rates of crystalloid in the most favorable Groups 1 and 2 compared to all patients undergoing open partial colectomy. Compared to 48% use in the All patients group (n = 307), Group 1 (n = 28) had 75% (p = 0.009) of patients with < 2000 cc. Group 2 (n = 18) had 70% (p = 0.084) and the combined Group 1 + 2 (n = 46) had 72% (p = 0.003) with intraoperative fluid restricted to < 2000 cc. We also analyzed the use of colloids and blood among colon surgery cases and found no significant differences. Albumin, hydroxyethyl starch, and blood transfusion utilization were low (< 13%) across all groups.

3.3 Readmission analysis

United States policy makers have defined readmissions as a costly and preventable quality of care metric [16]. We thus evaluated 30-day readmission trends in colectomy patients by comparing those with readmission to the entire group (Table 3). There were 144 patients (8.1%) of 1786 cases with readmission for any cause to the same hospital within 30 days. Several characteristics made it significantly more likely that a patient would experience readmission including emergency status for surgery, diagnosis of inflammatory bowel disease (IBD), diagnosis of diabetes, > 2000 ml intra-operative fluid and those receiving an excision procedure of the rectum. Interestingly, we found that one specific facility (Hospital location 13) performed particularly well. Across the hospital system, 8.1% of patients had a readmission but at Hospital location 13, only 1.4% of patients had readmission. We performed additional subset analysis of patients undergoing open partial colectomy. Similar readmission patterns were seen in this sub-cohort.

3.4 Inflammatory bowel disease versus colon cancer diagnosis

Colorectal surgery is commonly performed for inflammatory bowel disease (IBD) or colon cancer and the diagnosis can affect patient recovery and outcomes [17]. We examined the outcomes of patients with primary diagnoses of IBD and colon cancer (Table 4). We found no consistent trends in

Table 3 Readmission detail among all colectomy cases

Software discovered groups	Readmitted group n = 144/8.1% (%)	All colectomy n = 1786 (%)	P value
Emergency surgery status	**6.3**	2.5	0.013
IBD	45.8	36.0	0.030
Colon cancer	12.5	20.4	0.022
Diabetic	**13.2**	7.1	0.012
Voluven	13.9	11.4	0.342
Procedure type and location			
Excision procedure rectum (Code = 025)	**12.5**	6.4	0.009
Hospital (location 13)	1.4	8.1	0.001
Intra-op crystalloid fluids			
< 2000 cc	34.7	42.5	0.064

All inferences were two-tailed. Bold value represents the statistical significance at P = 0.05

IBD inflammatory bowel disease

Table 4 Inflammatory bowel disease IBD vs. colon cancer diagnosis

Software discovered groups	Patient cohort	LOS	Cost	Readmission (%)
Laparoscopic partial colectomy				
IBD	n = 95	5.64	Low	10.5
Colon cancer	n = 181	5.34	Low	6.1
Other (including rectal cancer)	n = 192	4.82	Low	3.6
Open partial colectomy				
IBD	n = 79	7.66	Medium	10.1
Colon cancer	n = 77	8.43	Medium	5.2
Other (including rectal cancer)	n = 149	9.38	High	10.7
All colectomy				
IBD	n = 643/36%	6.35	Medium	10.3
Colon cancer	n = 364/20.3%	6.03	Low	4.9
Other (including rectal cancer)	n = 779/43.6%	6.9	High	7.7

Cost cost of care for surgical episode, *IBD* inflammatory bowel disease, *LOS* length of stay

LOS or cost per case across three cohorts, laparoscopic partial colectomy, open partial colectomy and all colectomies. However, there were significantly higher rates of readmission among IBD patients compared to colon cancer in all three cohorts. The IBD patients were close to twice as likely to have readmission compared to colon cancer patients. In the "All patients" group, IBD patients had a 10.3% readmission rate versus 4.9% in colon cancer patients ($p = 0.002$).

4 Discussion

In this paper, we report our experience of utilizing machine intelligence to identify clinical variation and its impact on outcomes in colorectal surgery patients. We analyzed patient characteristics and interventions and their relationship with outcomes. Specifically, ketorolac use, intra-operative intravenous fluid use and patient diagnosis (IBD vs. cancer), and their association with outcomes—cost per case, length of stay and readmission rates-was analyzed. All findings were consistent with the current evidence. However, we reached the conclusion quickly using a machine intelligence based approach, in contrast to resource intensive prospective analysis. We studied multiple interventions of interest and completed the analysis over a relatively short two-week period of time which included approximately 10 h of analysis time.

By combining the machine-derived findings with domain knowledge of anesthesiology and surgical practice, we efficiently identified aspects of care with better outcomes. Although the presented findings are not novel discoveries, they provided prompt insight into our clinical practice. We realize that this analysis alone does not prove cause and effect of these care decisions and the outcomes. However, the real time data and analysis are valuable to create and optimize clinical pathways delivering actionable information to the clinician. The goal is not to allow every clinician to adopt a care strategy. The goal is to help care path development teams (clinicians) to adopt a more consistent care strategy for a group of patients, thus reducing variation in care provided.

We learned that this technology has several advantages over traditional analytic approaches:

1. Analysis across disparate data sets—the machine intelligence software enabled joining of four disparate data sets at the patient level for ease of analysis. In particular, we had never before had comparisons of cost per case or length of stay with data in our anesthesia record keeping system or postoperative medications and EMR problem list.
2. Unsupervised discovery—the software algorithms rapidly identified patients who had received similar care across numerous hospitals and identified the differentiating treatment pathways for each group of patients. Specific findings in our patient cohort support treatment recommendations in accordance with enhanced recovery pathways [12, 13]. Findings of specific similarities in groups with desired outcomes can be considered as a hypothesis generation for further investigations.
3. Speed and auto-generation of clinical pathways—we rapidly created a consensus clinical pathway from our best performing subgroups of patients. This has the potential to save substantial time in the updating of pathways and the creation of new pathways. Since the pathways are generated using real-world EMR data from across our multi-hospital system, the pathways have generalizability and can be recognized as practical.
4. Ease of use by team members—the software allows easy comparison of groups and sub-cohorts of patients across a wide range of categorical and continuous variables.

The auto-calculation of statistical significance makes identification of important trends intuitive. For example, we were able to identify important trends associated with intraoperative crystalloid use. We found that limiting the use to < 3,000 cc is associated with lower cost and LOS. This is consistent with evolving literature on restrictive or even "zero-balance" fluid management.

5. Adherence reporting—the system creates detailed reports at both the physician and hospital levels comparing performance against a selected consensus pathway. Reports can be used to focus attention on current use patterns for best practices across a wide range of topics (e.g. perioperative antibiotics, anesthetic choices, perioperative fluid management, surgical supplies, postoperative pain management, diet, patient activity, etc.). Keeping in mind that the most common cause of failure of ERAS pathways relates to providers' noncompliance with the protocols, direct and detailed feedback may be of particular importance. The ability to provide compliance feedback to providers may increase adherence to the clinical pathways and identify obstacles in effective and efficient execution of ERAS protocols.

5 Conclusion

The optimal set of interventions to be included in a care pathway can be difficult to define due to lack of high quality evidence. Our investigation indicates that machine intelligence can quickly identify clinical interventions associated with favorable outcomes. Insights from machine intelligence along with available scientific evidence can thus guide organization-specific care path development. Also, the technology enables adherence monitoring utilizing real-time healthcare data.

Author Contributions KM, JC, RA, TC: helped design the study, analyze the data, revise the article for scientific and intellectual content, and prepare the manuscript. PM, FXC: helped analyze the data, revise the article for scientific and intellectual content, and prepare the manuscript. DL, KR, AK, KCC: helped revise the article for scientific and intellectual content, and prepare the manuscript.

Compliance with ethical standards

Conflict of interest Francis X. Campion served as Chief Medical Officer for Ayasdi Inc during this project. None of the other authors have a personal financial interest in this work.

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