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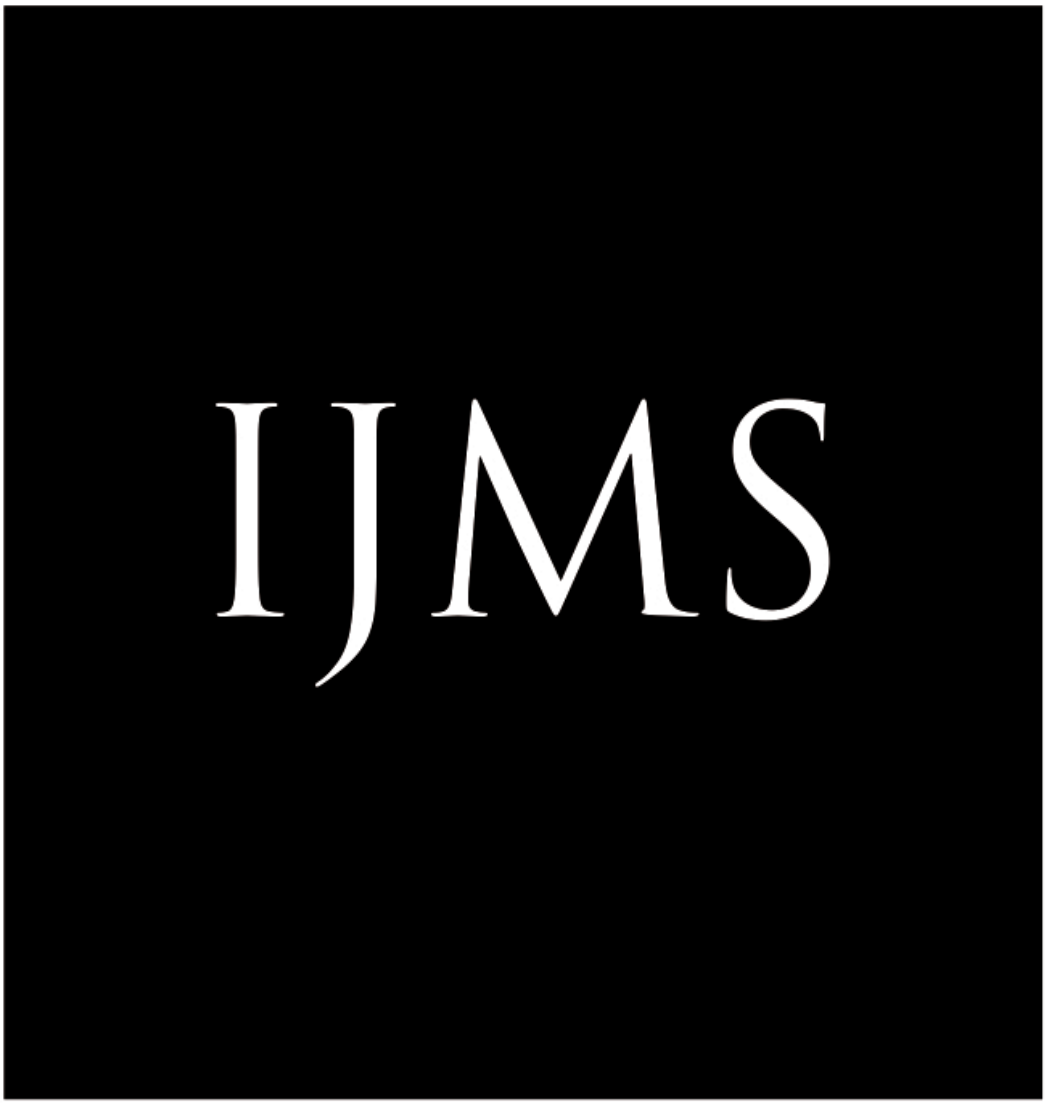

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The *International Journal of Medical Students* (IJMS) is a peer-reviewed open-access journal, created to share the scientific production and experiences of medical students worldwide.

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Original Article

Student Heart Failure Intervention Pilot: A Study of Risk Factor Analytics and Population Outreach

William Byron Reichert,[1,2] Gerard Hoatam,[2] Emily Schmidt,[2] Michael Leher,[2] Arathi Gorur,[2] Anna Jones,[2] Anantharam Kalya,[3] Priya Radhakrishnan.[2]

Abstract

Background: Heart failure, the leading cause of hospitalization in adults over the age of 65, is a difficult-to-treat syndrome associated with high morbidity and mortality. Home-monitoring programs may help reduce heart failure-associated morbidity but can be difficult to establish in smaller clinical settings. In this quality improvement project, we identified local patients at high risk of heart failure-related morbidity and hospitalizations, then implemented a medical student-based constant-contact program to encourage their follow-through on self-care. **Methods:** Between June 2012 and September 2014, our clinic treated 197 patients for systolic or diastolic heart failure. These patients' baseline characteristics were evaluated for trends that increased their risk for hospitalization. Of the high-risk patients identified (n=80), 12 (15%) were enrolled in the project. An 8-week constant-contact intervention was initiated through weekly calls. Patients' health statuses were recorded, and the importance of self-care was reiterated. **Results:** High-risk heart failure patients were identified based on >10 clinic visits during the study period; 3 were lost to follow-up. Each patient completed two questionnaires at the study's beginning and conclusion, with response rates of 67% (6/9) and 56% (5/9). Most participants reported symptom improvement and increased knowledge about their conditions. **Conclusion:** Our preliminary population-guided, medical-student-initiated intervention in a small clinical setting was designed to increase patient understanding and compliance and to improve heart failure symptoms. Although the study was limited by its low participation rate, drastic improvements in self-reported outcomes were noted among participants. A larger study with similar positive outcomes could ultimately influence follow-up methods.

Key Words: Heart Failure, Population Characteristics, Risk Assessment, Quality Improvement, Medical Student (Source: MeSH-NLM).

About the Author: *William Reichert completed his Medical Degree at Creighton University School of Medicine. He is currently training in Internal Medicine with hopes of pursuing a career in cardiology.*

Introduction

Heart failure (HF) affects an estimated 5.1 million individuals in the US and is the leading cause of hospitalization in adults over 65 years of age. [1, 2] Estimated costs associated with HF range from $37 to $39 billion annually. [3, 4] Current projections state by the year 2030, there will be an estimated 8 million people living with HF in the US, placing a tremendous burden on the national healthcare system. [5] Of equal concern is the fact that 5% of patients in the US healthcare system account for 59% of all national healthcare costs. [6] Recent decades have seen great efforts to drive down the cost of healthcare in the United States and identifying high-risk HF patients—so-called "super-utilizers" of healthcare resources—could facilitate the development of innovative programs that would reduce the costs associated with HF morbidity and hospital admissions. If these patients were more easily identified and more comprehensively educated, it could ease the strain on the national healthcare system.

Numerous innovative management programs have attempted to reduce the costs associated with caring for these super-utilizers. [7] One of the keys to implementing such programs involves the use of evidence-based data to identify this patient population—then, once they are identified, effective interventions must be established. [8] Ideally, these interventions should improve coordination of care and lessen the strain these super-utilizer patients place on the healthcare system. [9, 10] Although some progress has been made in this area, the characteristics of patients who would benefit from these targeted programs have not been specifically defined for every unique population, and the effectiveness of such efforts in small clinical settings is unknown due to inherent study size limitations. Numerous variables affect one's overall health, including psychosocial, race, gender, socioeconomic, mental health, and traditional risk factors. [11-15] Given the relative homogeneity of patients treated in small clinics for the same condition, it is important to develop programs that target their specific population to maximize the effect of their treatment. To maximize these potential benefits, a novel, small-clinic pilot program was founded with the goal of looking at HF patients specifically—a particularly important population.

Previous studies have described improved coordination of care and positive effects of increased patient education and at-home monitoring programs on HF morbidity and mortality, some reporting a 56% reduction in HF-related readmissions and a 44% reduction in readmissions for reasons unrelated to HF.[16-21] Given the complexity of HF patients and high hospital readmission rates, we designed a program at our academic medical center, which is a Level 3 National Committee for Quality Assurance-certified patient-centered medical home, to address the high morbidity rates associated with HF. Our program, named the Student Heart Failure Intervention Pilot (SHIP), was a medical-student implemented, population-based quality improvement program designed to identify and address unique social determinants responsible for HF-related hospitalizations in a local population. The main goal of this project was to improve

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morbidity in patients with HF and decrease the number of related hospitalizations through risk factor analysis and telehealth outreach programs. In addition to improving patient care, another goal of this program was to improve medical trainee longitudinal patient exposure by engaging medical students in the continuum of care under the close supervision of an attending physician.

Materials and Methods

This study was approved by the Institutional Review Board at St. Joseph's Hospital and Medical Center in Phoenix, Arizona and was designed based on Plan–Do–Study–Act protocols in a cross-sectional study design. The Quality Improvement SHIP team consisted of six medical students and an attending physician. The initial cross-sectional study used the Allscripts (Allscripts, Chicago, IL) Ambulatory Electronic Health Record registry to identify 197 patients diagnosed with systolic or diastolic HF at the Internal Medicine and Family Medicine clinics at St. Joseph's Hospital and Medical Center in Phoenix, Arizona, between June 2012 and September 2014 (***Table 1***). Baseline demographic information and comorbidities were assessed to identify risk factors for HF admissions in this cohort. The dataset was then cross-referenced with hospital admissions at St. Joseph's Hospital and Medical Center for patients with HF as primary diagnosis. In addition to the demographic data analyzed, we also analyzed income data obtained based on the average income of the neighborhood of each patient's home address. Demographics (including income data) were analyzed as variables, which were then compared between hospitalized and non-hospitalized patients. Number of clinic visits were found to be statistically significant and were used to identify high-risk patients: those who visited the clinic more than 10 times in the previous 2 years were identified as high-risk. Eighty of the 197 (46%) HF patients met this criterion; these high-risk patients were then contacted to participate in the intervention. Of the 80 high-risk patients identified, 12 agreed to participate in the intervention portion of the pilot, a longitudinal study, and informed consent was obtained. This intervention included medical students calling the high-risk patients on the telephone each week. Once the patients were enrolled, the medical students developed a standardized educational curriculum explaining the definition of HF, informing the patients about why it is important to closely monitor HF symptoms, and offering patients ways to maintain functional status under the guidance of (and based on recommendations from) the supervising faculty. These topics were discussed with patients during weekly calls for the duration of the project (minimum of 3 attempts per week); in addition to the informational component of these phone calls, the medical students also asked patients questions about their symptoms and about their understanding of the HF curriculum. We hypothesized that diligent follow-through and independent care would improve patients' knowledge about HF, thus decreasing morbidity and rate of hospital readmissions. The patients' responses were recorded, along with the duration of each call. Three patients were lost to follow-up. Each patient was given the Minnesota Living with Heart Failure Questionnaire (MLHFQ) at the beginning and end of the study, with a response rate of 67% (6/9). Patients also completed a patient preference questionnaire (PPQ), based on established telemedicine satisfaction questionnaires, with a response rate of 56% (5/9). [22] A minimum of three attempts were also made to secure end-of-study questionnaires from each patient.

The unpaired t-test was selected to evaluate the baseline demographics and potential risk factors to compare the means of the two (hospitalized and non-hospitalized) independent groups. This was performed under the assumption of identically distributed samples. Given the small number of participants, only probability values were calculated for statistical analysis at study completion.

Results

Our program reviewed treatment of 197 patients diagnosed with HF over a two-year period. Hospital admission data were tracked between September 1st, 2013 and September 30th, 2014. During that time, 19 of the 197 HF patients were admitted to the hospital (14 had single visits, 5 had multiple visits). There was a significant difference in the number of clinic visits between the 19 hospitalized clinic patients (mean, 16.89 ± 14.58 visits) and the 178 non-hospitalized clinic patients (mean, 10.38 ± 9.75 clinic visits; $t(195)=2.6195$ $p<0.0095$). This benchmark was used to classify patients at high-risk of HF-related readmission to the hospital. Additional variables assessed can be found in ***Table 1***. Of the hospitalized patients for whom income data were available, 47% (8/17) had a household that earned less than $40,000/year; 53% of patients (9/17) had an annual income between $40,000/year and $70,000/year. No hospitalized patients had earnings of more than $70,000/year. This trend was also seen in average number of clinic visits - that is, lower income was correlated with more frequent visits to our clinic (mean clinic visits for <$40,000, $40,000 - $70,000, and >$70,000 annual income was 11, 12, and 5, respectively). Three patients were lost to follow-up during the duration of the program. Of the 3 patients lost to follow-up, 2 never completed a weekly telephone call while the third completed 2 phone calls (of 8 attempts). All 3 patients were counted as lost to follow-up due to their failure to answer or return phone calls; no patient formally withdrew from the study. These patients' data were excluded from all parts of the results, but their baseline demographic data were included in the initial risk analysis.

Responses to the MLHFQ collected after the program's conclusion indicated overall symptom improvement with an average decrease in score of 9 points out of 105 possible points (with lower scores being more desirable; 44.3 ± 34 to 35 ± 26). Before the study, 6 patients were unable to describe the definition of HF to the medical student, could not understand the importance of follow-through on physician instructions, or articulate steps to monitor HF; by the study conclusion, 5 of those 6 patients (83%) were able to convey an understanding of HF and were successful in describing the importance of HF monitoring. Most of the symptomatic patients in the study (7/8; 88%) reported symptom improvement in at least 1 of the following categories: presence of orthopnea, chest pain, pre-syncope, edema, fatigue, or cough.

Responses to the PPQ showed a minimal increase in preference for phone calls from surveyors, from a mean score of 41 ± 9 points at the study outset to 43 ± 11 at the study conclusion. No single participant reported 100% compliance with physician directives (i.e., smoking cessation, recording weight and blood pressure daily). ***Table 2*** summarizes additional results from the intervention portion of the study.

Table 1. Demographics of Hospitalized, Non-hospitalized, and Study Patients. Data are expressed as n (%), unless indicated otherwise. †One of the nine study patients was recruited from the hospital (not a clinic patient) and therefore was not included in baseline characteristics.

Variable		Hospitalized (n=19)	Non-Hospitalized (n=178)	Total (n=197)	p-value	Study (n=8)
Sex	Male	11 (58)	87 (49)	98 (50)		3 (38)
	Female	8 (42)	91 (51)	99 (50)		5 (63)
Mean age, years		65 ± 13	66 ± 15	66 ± 15	(p=0.26)	67 ± 12
Mean BMI, kg/m²		32 ± 9	32 ± 10	32 ± 10	(p>.99)	36 ± 12
Under- or uninsured		17 (89)	120 (67)	137 (70)		3 (38)
Race	White	10 (53)	103 (58)	113 (57)		6 (75)
	Black	3 (16)	19 (11)	22 (11)		0 (0)
	Hispanic	5 (26)	37 (21)	42 (21)		2 (25)
Comorbidities	COPD	4 (21)	41 (23)	45 (23)		3 (38)
	CAD	8 (42)	55 (31)	63 (32)		1 (13)
	T2DM	7 (37)	76 (43)	83 (42)		3 (38)
	Hypertension	15 (79)	101 (57)	116 (59)		2 (25)
Mean number of medications		14 ± 7	14 ± 7	14 ± 7	(p>.99)	15 ± 2
Beta blocker		15 (79)	114 (64)	129 (65)		7 (88)
ACE/ARB		17 (89)	102 (52)	85 (43)		4 (50)
Furosemide		9 (47)	109 (61)	118 (60)		4 (50)
Employment status	Unemployed	7 (37)	45 (25)	52 (26)		1 (13)
	Employed	2 (11)	25 (14)	27 (14)		2 (25)
	Retired	10 (53)	77 (43)	87 (44)		5 (63)
Marital status	Married	6 (32)	58 (33)	64 (32)		2 (25)
	Single	12 (63)	82 (46)	94 (48)		5 (63)
	Divorced	1 (5)	16 (9)	17 (9)		1 (13)
	Widowed	0 (0)	19 (11)	19 (10)		0 (0)
	Deceased	2 (11)	23 (13)	25 (13)		0 (0)

Table 2. Characteristics of HF Patients Enrolled in SHIP. * Twelve patients were initially enrolled in SHIP; 3 were lost to follow-up and were not included in the table. † Data are presented as n (%), unless otherwise specified. ‡ Understanding was defined as medication compliance, ability to recall prescribed medications, and standardized general HF knowledge. § Recorded only if patient was consuming vegetables less than 2 days per week at enrollment. ‖ Symptoms are defined as subjective chest pain, dizziness, swelling, fatigue, and/or cough. ¶ Denominator is 8 as one patient did not have symptoms/lack of understanding at trial start.

Characteristic	n (%)†
Mean age, years	69 ± 13
Male sex	4 (44.4)
NYHA Class I	2 (22.2)
NYHA Class II	3 (33.3)
NYHA Class III	4 (44.4)
Mean daily medications ± SD	16.8 ± 3.6
Mean daily cardiac medications ± SD	2.8 ± 1.1
HF-related hospitalizations (previous year) for enrolled patients	2 (22.2)
HF-related hospitalizations (during SHIP) for enrolled patients	2 (22.2)
Symptomatic patients at time of SHIP enrollment	8 (88.9)
Symptomatic patients who reported improvement at SHIP conclusion	7/8¶ (87.5)
Patients who reported lack of understanding at time of SHIP enrollment‡	6/9 (66.6)
Patients who had a gap in understanding who later reported increased understanding	5/6¶ (83.3)
Mean increased in fresh vegetable consumption (days per week)§ ± SD	4.4 ± 1.1
Constant contact	
Mean no. of telephone calls completed during study ± SD	6.2 ± 1.6
Mean completed telephone calls when HF symptoms changed ± SD	4.9 ± 1.9
Mean completed telephone calls until understanding changed ± SD	3.6 ± 1.3

Discussions

Many traditional risk factors for HF-related hospitalization (e.g., diabetes mellitus, New York Heart Association functional class, etc.) have been established; however, we sought to identify simpler, less-invasive risk factors in our patients.[23-27] Higher utilization of primary care visits had an inverse relationship to likelihood of hospitalization and was included in this study to identify patients at increased risk of hospitalization, as discussed above. Although the data were not statistically significant, several additional risk factors were identified: income level, insurance status, number of comorbidities, and gender. This program illustrates the importance of understanding the social determinants of health while developing programs for the chronically ill.

Patient participation was a limitation of this study, with 68 of the 80 high-risk patients being either unable or unwilling to be included in this study. This limited the effectiveness of the study in our clinic as a whole but did provide a proof-of-concept for future programs. The difficulty our group experienced in enrolling patients drives home the importance of discussing critical aspects of self-care during traditional clinic visits or before hospital discharge and enrolling patients in the program at that time. These small numbers also limited the statistical significance of the patient demographics (except the number of clinic visits in relation to hospitalizations), though an easily identifiable risk factor was nonetheless identified for our specific patient population. Additional confounders include the capabilities of each medical student who provided patient education, but this was minimized by providing medical students with a standardized curriculum that had been developed with the assistance of the supervising physician. We were unable to identify a study similar to ours, as many modern population analysis projects rely on large data or meta-analyses to generate statistical significance.

This study is also subject to an inherent selection bias, as those willing to participate in the program may have been more inclined to complete their education and to make positive lifestyle changes, regardless of follow-up calls and reminders from the medical students. If inclusion in the study included the entire HF population of this clinic, this bias may be reduced. In addition, participants in this study had a wide variety of educational backgrounds: some had only completed some secondary education, whereas others had completed postgraduate training.

Despite these limitations, the results of our SHIP program show that establishing a HF-directed constant-contact plan is feasible in a small clinical setting and a unique risk factor may be elucidated for a specific clinic population. The constant-contact program was successful in educating patients on self-management using a standardized curriculum. The duration of the pilot was established taking into account the known fact that high-risk patients with HF are admitted and readmitted to the hospital at a higher rate than patients with other medical conditions. One study showed that patients with HF had a 25% chance of being readmitted to the hospital within 30 days of their most recent hospital discharge.[18] Given that short timeframe, an 8-week duration was chosen for this pilot, to expedite data gathering while also allowing sufficient time to detect re-hospitalization. Given the low number of hospitalizations, this timeframe was likely insufficient to capture enough data to confirm whether the education program was effective in lowering HF-related hospitalizations.

Medical students were the point persons in this study; however, others have reported that trained nursing staff can also carry out regularly scheduled phone calls following hospital discharge.[28-30]

These studies confirm that such programs can help decrease the number of hospital admissions and improve quality of life. If outreach resources are limited, such programs may improve HF-related care costs in populations without access to "big-data", or whose populations do not fit into larger data analyses by using smaller risk analyses. In addition to the benefit of this program on patients, our program highlights the opportunity to engage medical students in an innovative patient-continuity experience in population health, while simultaneously offering them training on how to develop and implement a Quality Improvement study. This allowed the medical students additional longitudinal patient contact - something of a rarity for many medical students - and provided them concrete feedback that the interventions they advocated were directly benefitting patients.

Future study should involve implementation of such a program on a larger scale to identify statistically significant trends in this population and to validate frequent clinic visits as a risk factor for hospitalization (both initial hospitalizations and hospital readmissions). Once initial lifestyle changes are made, some patients may require additional motivation and support to achieve - and maintain - positive, long-term lifestyle changes, hence engaging HF patients via a constant contact program may prove successful in caring for such patients.

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Review

A Systematic Review of Cerebral Arteriovenous Malformation Management

Karen Eliahu, [1] Florence Hofman, [2] Steven Giannotta. [3]

Abstract

Cerebral Arteriovenous Malformation is a neurovascular lesion characterized by an abnormal connection between arterial and venous systems, resulting in a tangle of blood vessels lacking intervening capillaries. The goal of treatment is to prevent catastrophic hemorrhage, neurological injury, or death. Despite the availability of multiple cutting-edge treatment options there is little consensus on the most promising approaches for treatment due to the novelty of each Arteriovenous Malformation case. This analysis will link the various angioarchitectural characteristics and associated presentations of Arteriovenous Malformation to treatment modalities. In the era of personalized medicine, genomics-driven research to normalize by drawing parallels between Cerebral Cavernous Malformation and Arteriovenous Malformation, both of which are characterized by hemorrhage-prone vascular malformations, may provide insight for the development of pharmacological therapy. Understanding the underlying mechanisms and genes responsible for the symptoms will allow us to better treat patients in a non-invasive manner and paves future directions in Arteriovenous Malformation treatment.

Key words: Intracranial Arteriovenous Malformations, Hemangioma, Cavernous, Central Nervous System, Precision Medicine, Gene Knockout Techniques, Patient Selection (Source: MeSH-NLM).

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Introduction

Symptom heterogeneity of a single disease is one of the most compelling aspects of medicine. This phenomenon requires a case-by-case analysis of each patient as well as a novel approach for treatment. Brain Arteriovenous Malformation (AVM) illustrates this concept due the diversity in structure of the vascular lesions. Detection of AVM frequently occurs in acute situations; at the time of diagnosis approximately two-thirds of patients present with intracranial hemorrhage, 15% of patients are asymptomatic and about 20% experience seizures highlighting the lack of a "typical" presentation. [1-3]

Variable factors such as the location, size, and angioarchitecture of the tangle of blood vessels (nidus) pose a significant challenge for diagnosis and treatment. These connections that make up the nidus are problematic as they result in high-flow circulatory shunting of blood from arterial to venous systems, leading to hemodynamic abnormalities which are the origin of disease. [1, 4]

Methods

In this review, a variety sources were synthesized to explore our current knowledge of the treatment and management of AVM as well as information about future directions for treatment. The PubMed Database was searched for significant studies and relevant discussions from peer reviewed journals in the field of AVM. Searched terms included: Intracranial Arteriovenous Malformations, Hemangioma, Cavernous, Central Nervous System, Cerebral Angiography, Endothelial Cells, Endovascular Procedure, Gene Knockout Techniques, Intracranial Hemorrhage, Microsurgery, MicroRNAs, and Radiosurgery. References of sources were used to identify additional sources. Relevant discussions included longstanding questions about the value of therapeutic abstention and more recent discussions about patient selection and the value of using newer endovascular techniques or Gamma Knife radiosurgery over the older traditional surgical techniques. As these questions evolved over time several opinions emerged to answer these difficult questions. As a result, we included traditional opinions that have played a large impact in the determination of standard of care and recent opinions ranging from 1986-2016. Furthermore, to provide a solid background about the epidemiology of the disease we found it useful to include a variety of sources because of the widespread disagreement on statistical figures associated with AVM. Sources from 1966-2016 were used and sources that followed several hundreds of patients were given value because of the lack of this type of large scale study.

AVM research is underdeveloped with fewer long-term and large-scale studies when compared to similar the number of studies existing for similar vascular malformations and as a result a wider net must be cast to ensure an accurate representation of statistical figures. When discussing recent and future research directions such as normalizing vasculature and using gene knockout techniques we included sources from 2000-2016 as sources and focused literature search to several studies whose main purpose was to normalize vasculature. Studies that included but did not primarily focus on normalizing vasculature were excluded. To minimize the risk of bias, several conflicting opinions were chosen when discussing popular debates in AVM treatment such as therapeutic abstention and patient selection. Varying opinions about statistical figures were also used and noted in the epidemiology section and sections

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examining the link between angioarchitecture characteristics and clinical presentation in order to fairly and accurately examine multiple angles of these important discussion. Papers in English or papers with an English translation were chosen.

Related Disorders

Cerebral Cavernous Malformations (CCMs) are vascular lesions that are characterized by slow low perfusion and are known to be angiographically occult.[5] Dural arteriovenous fistulas consist of fistulas between dural arteries and dural veins or venous sinuses and may contribute to the development of tinnitus and high-flow vascular shunts leading to hemorrhage risk. [6, 7] Pial arteriovenous fistulas are characterized by single or multiple pial or cortical arterial connections to a single venous channel and differ from AVMs by the lack of a true nidus. [8]

Cerebral Proliferative Angiopathy is identified by the presence of several small arterial feeding vessels and draining veins with normal brain parenchyma observed in-between abnormal vessels of the nidus. [9] Moyamoya Disease is defined as a progressive stenosis or occlusion of the internal carotid artery often leading to ischemic effects that cause development of a characteristic collateral network of vessels resembling a puff of smoke which translates to "moyamoya" in Japanese to compensate for reduced cerebral perfusion. [10] Vein of Galen aneurysmal malformation angiopathy is characterized by one or more arteriovenous shunts that drain into a dilated vein of Markowski, the embryonic precursor to the Vein of Galen, often resulting in heart failure in the pediatric population. [11]

Epidemiology

The incidence of AVM is approximately 1 in 100,000, the prevalence is approximately 18 in 100,000, and the annual fatality risk is 1–1.5%; these values are approximations as a large number of asymptomatic patients are not accounted for. [1, 12, 13] The crude annual risk of a hemorrhage is about 2-4%. [2, 14-20] Great variability of individual fatality risk exists due to AVM characteristics such as arterial feeding blood flow and venous drainage pattern. Each hemorrhage a patient experiences may severely impact quality of life and basic functionality.

AVMs are the leading cause of non-traumatic intracerebral hemorrhage in individuals aged younger than 35 years old. [21] There exists, however, much disagreement about the proportion of strokes and hemorrhage that AVMs cause, some estimates account AVMs as the cause of 1% to up to one-third of strokes and 4% to one-third of primary intracerebral hemorrhage in adults. [1, 2, 4, 12, 17] Recurrent hemorrhage is an ongoing risk of AVM and is estimated to be as high as 17-18% in the first year although some suggest lower rate of risk.[1, 17, 20] Morbidity resulting from rupture has been reported to be as high as 53% to 81% and mortality has been noted from 10% to 17.6% highlighting the need for early detection, treatment of AVM prior to rupture, as well as increasingly effective methods to treat rupture.[14, 22, 23] Of all AVM-related hemorrhages, 63% are intraparenchymal, 32% are subarachnoid, and 6% are intraventricular.[24]

Female gender is associated with significant hemorrhage risk while male gender is associated with presentation of seizures.[25, 26] The mean age of diagnosis is 27.9-32 years and hemorrhage risk peaks at a younger age (29 years and below).[26, 27] Hemorrhage risk decreases over time except after the age of 60 where it begins to increase.[26] Non-white race is significantly associated with hemorrhagic presentation as well.[27]

Genetic Influences in AVM

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is an autosomal dominant genetic disease associated with a spectrum of vascular malformations.[28, 29] Nine to 16% of patients with HHT are diagnosed with brain AVMs.[29] Patients diagnosed with HHT1 have a higher prevalence of brain AVMs than the general population and patients with other types of HTT.[28] Generally AVMs occur sporadically; only 2% are familial.[30-33]

AVM is caused by TGF-β (Transforming growth factor beta) genes experiencing a loss of function mutation; these genes are implicated in cell proliferation, differentiation, morphogenesis, tissue homeostasis, regeneration, and epithelial-mesenchymal transition.[13, 34-37] A mutation in endoglin, a gene involved in angiogenesis, is the cause of type 1 hereditary hemorrhagic telangiectasia (HHT1).[28] Endoglin encodes an accessory protein of TGF-β receptor complexes.[13] Type 2 hereditary hemorrhagic telangiectasia (HHT2) is characterized by a mutation in activin-like kinase 1 (ALK1, or ACVLR1), which codes for a transmembrane kinase also suspected to participate in the TGF-β signaling pathway.[13]

Pathophysiology

Understanding the angioarchitecture of AVMs is vital to the investigation of the etiology of associated hemorrhage, arguably the most concerning pathophysiologic symptom. The anomalous tangle of vessels results in irregular blood flow such that high blood flow is initiated in the feeding artery and carries through directly to the vein causing complications as veins are characteristically low pressure blood vessels.[38] The lack of capillaries allows shunting of blood at a high speed and volume from the arterial system to the venous system. This consequent irregular blood flow results in weaknesses in blood vessel junctions, without the dissipation of pressure in the capillary system which results in risk of aneurysm development and rupture.[39] Further complications arise because nidus vessel walls are often thin and constituent arteries lack a muscularis layer; as a result blood flow cannot be regulated within the artery.[23, 40]

Often shunting results in diversion of arterial supply to local brain tissue known as "steal" phenomena which may result debilitating ischemia and life-threatening hemorrhagic stroke. [23, 40]

Clinical Presentation

Diagnosed AVMs may present with intracranial hemorrhage (experienced by 43.4% of patients), seizure (17.3%), and headache (24.9%). [3, 41] Clinical outcomes are unique to each patient and are subject to nidus characteristics. Studied relationships exists between angioarchitectural characteristics and clinical symptoms (***Table 1***).

66% of AVM patients experience documented learning disorders which suggests the potential benefit of addressing functional cerebral deficits as a possible symptom to look for in the diagnosis process.[23] Although not every symptom associated with AVM will lead to an AVM diagnosis, some symptoms such as unexplained delays in learning may serve as a signal for physician to utilize additional diagnostic methods, such as imaging, for further investigation.

Diagnostic Imaging

Radioanatomic characterization of AVM through imaging yields important information that impacts the selection of treatment modality. [3, 42] As imaging has improved over time, diagnosis of AVMs has increased, creating additional challenges for treatment as a variety of AVMs are uncovered, often coincidentally. [43]

Table 1. Relationship between Angioarchitectural Characteristics and Symptoms.

Clinical Symptom	Angioarchitectural Characteristics
Intracranial hemorrhage	Intranidal aneurysm*, venous stenosis, exclusive deep venous drainage, single draining vein, high feeding mean arterial pressure, small nidus size*, deep location* [80, 81]
Cardiac insufficiency or developmental delay in children	High-flow shunting [82, 83]
Dementia	Increased vascular resistance secondary to a long draining vein [18]
Seizures	Venous varices in venous drainage [84]
Clinical symptom	Angioarchitectural Characteristics
Intracranial hemorrhage	Intranidal aneurysm*, venous stenosis, exclusive deep venous drainage, single draining vein, high feeding mean arterial pressure, small nidus size*, deep location* [80, 81]
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Computerized tomography is used as a confirmation tool for identifying the location and extent of a hemorrhage.[3] Magnetic resonance imaging provides the greatest visualization that illustrates the relationship between the lesion and the local brain tissue adjacent to the nidus.[3, 42, 43] Arterial spin labeling magnetic resonance imaging is often used to diagnose arteriovenous shunts without true nidus to determine if the vascular abnormality is truly an AVM or if the lesion is indicative of a different disease. [38, 44]

Digital subtraction angiography is the gold standard for the evaluation of angioarchitecture of AVMs; It shows the following essential features: the feeding arteries, location of nidus, draining veins, morphology, presence, and location of associated aneurysms, venous varices, and vasculopathic stenotic segments on arteries and veins.[3, 38, 42, 43]

Therapeutic abstention

Therapeutic abstention is proposed for asymptomatic multiple AVMs discovered incidentally without angiographic bleeding risk and in some cases where the nidus exists in eloquent areas.[45] Therapeutic abstention is often coupled with management of hypertension, conventional regimens for headaches, anticonvulsant medication to manage seizures and routine monitoring with surveillance imaging .[42, 43]

In acutely ruptured AVMs, temporary therapeutic abstention is crucial for healing before implementing invasive treatment options.[4] It is standard to wait a month or longer to allow for patient recovery, hematoma liquefaction, and inflammatory reactions to subside.[4] The only exception to the guideline is for superficial low Spetzler-Martin grade AVMs with elucidated angioarchitecture where it is feasible to perform a hematoma evacuation and excision of the nidus simultaneously. [4]

The Spetzler-Martin scale is a grading system used to predict surgical resection risk based on the nidus size, venous drainage pattern, and location in relation to eloquent cortex (site includes sensorimotor, language, visual cortex, hypothalamus, thalamus, internal capsule, brainstem, cerebellar peduncles, and cerebellar nuclei. [3, 43, 46] Higher grades are associated with greater surgical morbidity and mortality. [42, 43, 46]

The ARUBA Study: A Randomized Trial of Unruptured Brain AVMs (ARUBA) played a large role in determining whether it is worthwhile to treat AVMs based on the risks of the various treatment options available. The Rational for the ARUBA Study was designed to test the null hypothesis that treatment, by means of interventional procedures, surgery, or radiotherapy, offers no difference in the risk of death or symptomatic stroke, and no better functional outcome than does conservative management at 5 years from discovery of an unruptured brain AVM. [23, 47] The ARUBA Study findings are strongly oriented towards therapeutic abstention. [48] It is difficult to predict patient prognosis for therapeutic abstention because the ARUBA study is subject to several experimental flaws. [23, 49, 50]

Selection bias remains an issue with the ARUBA trial design, while it is a randomized control trial, only those patients deemed by their physicians to have low risk of hemorrhage will be enrolled because the standard of care for a high hemorrhage risk patient is to implement a more invasive therapeutic modality, thus compromising the ability of the study to represent a generalized AVM patient population. [23, 42] It is suggested that if death or stroke occurs a few years following a multimodal treatment then the treatment was in only fact partially completed and is therefore an ineffective and dangerous method. [48] It has been thought, contrary to the findings of the ARUBA study, that microsurgery, specifically on unruptured lesions smaller than 3 cm or on Spetzler-Martin Grade I and II lesions, leads to better outcomes when compared to therapeutic abstention or conservative treatments.[51] This finding was credited to well-selected microsurgical cases and suggests that improved patient selection will lead to improved outcomes. [51]

Treatment

AVMs are heterogeneous pathological entities and therefore require a unique multidisciplinary approach for treatment. [23] Accurate assessment of risk associated with treatment is crucial for achieving the best outcomes for patients. [52] Comparison of treatments must take into account the associated benefits and risks of each, is outlined in ***Table 2***. The risk of rupture has become the driving force for using multimodal therapies involving microsurgical resection, stereotactic radiotherapy, and endovascular embolization to obliterate lesions. [23]

Endovascular Embolization

Advances in endovascular technologies, including microcatheter design, and the development of liquid embolics with unique properties, have increased popularity of endovascular treatment, enabling the delivery of therapy despite the structural complexity of tangled blood vessels.[42]

An almost all cases, preoperative embolization is performed before surgical resection or stereotactic radiotherapy.[18] Preoperative embolization is often used to reduce the size of an AVM for microsurgical excision; the 6.5% complication rate is deemed low enough for utilization of this method.[18, 43, 53]

The most frequently used agents include the liquid embolic agents; n-Butyl Cyanoacrylate (n-BCA) and Onyx (an ethylene vinyl alcohol copolymer), used to block blood flow before surgical treatment.23 Appropriate patient selection is key to an optimal embolization treatment that prevents recurrent hemorrhage. AVM characteristics must follow specific guidelines in order for the treatment to reduce risk of rupture and not create additional disability for the patient. Criteria for embolization includes a small nidus size. [18] If a lesion exists within eloquent tissue, the role of endovascular therapy may be limited as the risk of stroke or ischemia may outweigh the benefits of treatment. [18]

Cases presenting with hemorrhage, deep venous drainage or associated aneurysms do not have a reduced risk of repeated rupture if only partially treated with this modality. [41]

Endovascular techniques can be applied to occlude intranidal and distal flow-related aneurysms and used for 'sealing' a rupture site or focal angioarchitectural weakness when the area of interest can be easily identified and safely accessed. [4]

The advantages of endovascular therapy include immediate occlusion in some cases, intraprocedural angiographic evaluation, and the utilization of a variation of viscosities of embolic agents which may be used for diverse angioarchitectural characteristics.[23, 42, 43] The disadvantages of endovascular therapy include the risks of partial embolization, unintended vessel embolization, intracranial hemorrhage, and normal perfusion pressure breakthrough, which may lead to edema or hemorrhage. [42, 43] As technology improves, this treatment modality may continue transition from a adjunctive therapy to a curative modality. [23] Novel techniques such as the transvenous approach, modeled after successful treatment techniques for dural arteriovenous fistulas, may make it possible to treat difficult high-flow cases with solely endovascular techniques.[54]

Stereotactic Radiosurgery

Gamma Knife radiosurgery (GKRS) is performed by administering sharply localized high-dose radiation to promote a vascular injury response with the goal of obliterating the vessel, a process often taking 1 to 2 years.[42] GKRS's strength lies in its precision as it affords submillimeter targeting and allows treatment in deep locations of the brain with minimal radiation exposure to neighboring brain tissue.[23]

As a result of this treatment modality's timeline, this treatment is not appropriate in acutely ruptured AVMs as therapeutic effects may not appear until after a number of months.[4] Small AVMs (less than 3-3.5 cm^3) are optimal for treatment and diffuse AVMs pose a significant challenge as it becomes harder to minimize interspace parenchymal tissue exposure to radiation in. [42, 55] A multicenter analysis of 1255 patients receiving GKRS reported 8% of patients who developed a neurologic deficit after the radiation treatment as a result of edema and necrosis of healthy brain tissue. [42, 56] Nevertheless, cure rates for AVMs treated with primary GKRS have been estimated at 80% at 2-year follow-up, highlighting the efficacy of GKRS as a less invasive solution than surgery to treating complexly shaped AVMs as well as AVMs in eloquent areas. [23]

Microsurgical Resection

Microsurgical resection with angiographic confirmation of obliteration are considered the gold standard of AVM treatment and are regarded as curative. [43, 57] Microsurgical technique has improved over time and has solidified itself as the best choice for patients with cerebral AVM if angioarchitectural characteristics are appropriate (non-diffuse lesions) and if manipulation of the location near the nidus would not cause severe complications.[3, 57] Symptoms often resolve dramatically following microsurgical resection of the AVM. [3]

The high rate of complete obliteration is the most notable advantage of this treatment modality, while the limitations of this approach include its invasiveness, anatomic accessibility, edema from retraction, intraoperative rupture, resection of normal brain tissue, feeding vessel thrombosis and infection risk. [3, 42, 43] A high cure rate has been associated with microsurgery in pediatric patients. [58] Furthermore, patients with AVMs smaller than 3 cm^3 experience better outcomes that include a lower rate of significant neurological deficits as a result of the surgery. [51]

Pharmacological Intervention Normalizes AVM Vasculature to Reduce Hemorrhage Risk

Current AVM research sheds light on potential for targeted noninvasive therapeutic modalities that aim to normalize AVM vasculature which reduces hemorrhagic risk. [59] Normalization of the vasculature is achieved by normalizing the abnormal levels of growth factors in AVM brain endothelial cells (BECs). There are several differences between healthy brain endothelial cells and AVM-BECs that may unlock the key to developing additional specific therapies based on molecular mechanisms of AVM-BECs.

Table 2. Relationship between Treatment Modalities and Angioarchitectural Characteristics.

Modality	Relationship to other modalities	Angioarchitectural characteristics
Endovascular embolization	Multimodal approach that renders surgery technically simpler or reduces size of large AVMs [85, 86]	Nidus with adjunct aneurysm(s) [55], multiple draining veins (transvenous approach) [54], small and medium sized AVMs [87], AVMs in posterior fossa (multimodal treatment) [88]
Radiotherapy	Effective as a standalone therapy, multimodal approach for partially embolized small AVMs [55, 85, 89]	AVMs less than 3-3.5 cm^3 in eloquent area [42, 55], less than 10-11 cm^3 in noneloquent area [89], high marginal dose of 16-25 Gy [55, 89], smaller target volume [55], fewer draining veins [55]
Surgical resection	Effective as curative modality [58], multimodal approach often following preoperative endovascular embolization[85]	AVMs smaller than 3 cm^3 [51], surgically accessible [58], superficial [85], noneloquent area [85], avoid deep draining veins and high-flow shunts [85]

AVM-BECs have been found to exhibit functional abnormalities in migration and tubule formation resembling cells in active angiogenesis.[59] The role of vascular endothelial growth factor (VEGF), a crucial proangiogenic mediator, has also been studied in AVM-BECs and it has been found that these cells are demonstrated to be "activated" when compared to normal BECs. [59] AVM-BECs have increased proangiogenic cytokine secretion and proangiogenic receptor expression indicating that they exist in an abnormal vascular growth state. [59] The subsequent elevation in the secretion of VEGF stimulates survival, proliferation, and migration which in turn may contribute to clinical outcomes that contribute to the challenges in treating AVM. [59] Further study must be done to determine if the abnormal characteristics of AVM-BECs are a result of their inherent differences from normal BECs or if they are characteristics that developed as a reaction to abnormal blood flow and ischemia caused by the malformation itself. [59]

One study was aimed at using microRNA-18a (miR-18a) as a therapeutic agent to improve AVM-BEC function. [60] It was found that the presence of miR-18a increased an important angiostatic factor that is downregulated in normal AVM-ECs production.[12, 60] Furthermore, miR-18a reduced VEGF levels which are both overexpressed in normal AVM-BECs, thus helping to normalize

the vascular cells.[60, 61] It was found by another study that upregulating thrombospondin-1 in AVM-ECs normalizes the rate of proliferation, migration, and the efficiency of tubule formation causing the AVM-ECs to resemble normal ECs.[61]

Ago-2 has been found to act as a systemic miR-18a carrier which facilitates miR-18a entry into brain endothelial cells in-vitro and in-vivo.[62] miR-18a, with the help of the Ago-2 delivery platform, have been shown to ameliorate key abnormal characteristics of AVM-BECs. [60-62] There is potential to develop pharmacological treatment for AVM that targets AVM-BECs, a cell type common in all AVM lesions, as a non-invasive method that would be compatible with diverse angioarchitectural characteristics and may be especially beneficial to patients with AVMs in eloquent area where invasive treatments may not be suitable.

Additionally, Notch4, may be a compelling molecular target to normalize AVM cells. Notch4 is a vascular angiogenesis regulator primarily found in endothelial cells and is implicated in initiation and maintenance of arteriovenous communications.[63, 64] In AVM, Notch4 is found to be overexpressed by up to 35%.[64] Normalization of Notch4 by repressing Notch4 expression has been shown to regress high-flow arteriovenous shunts.[40] This causes blood to return to capillaries resulting in a reversal of tissue hypoxia caused by "steal" phenomenon that often occurs in AVM.[40] Normalizing Notch4 in endothelial cells may be the key to overcoming the challenge of treating a heterogeneous population of lesions.

Drawing Parallels from Genetic Manipulations in Cerebral Cavernous Malformation Research

Recent strides in Cerebral Cavernous Malformation research using genetic manipulation in murine models may provide long awaited answers in AVM and may contribute to future development of pharmacological therapy for the disease. Cerebral Cavernous Malformation (CCM) is a vascular malformation that like AVM, is characterized by enlarged capillary cavities lacking intervening neural tissue and smooth muscle cells. [65, 66] Drawing parallels between CCM and AVM, both of which are characterized by hemorrhage-prone vascular malformations, may advance genomics-driven innovations within AVM research in the era of personalized medicine.

Normalizing CCM vasculature may be achieved by investigating the genes that cause abnormal vasculature. CCM vascular phenotype can be induced in murine models by endothelium-specific loss-of-function mutations of either of the independent genes; CCM1 (also known as KRIT1) CCM2 (OSM) and CCM3 (PDCD10). [67-70] CCM3-deficient endothelium takes on mesenchymal- and stem-cell-like characteristics (EndMT) and as a result, the transforming growth factor (TGF-β) pathway becomes activated, contributing to the development of vascular malformations. [68, 70] The anti-inflammatory drugs sulindac sulfide and sulindac sulfone have been shown to reduce the number and size vascular malformations in CCM3-deficient cells by inhibiting TGF-β. [68] Further studies have shown EndMT switch occurs in sporadic CCM patients and that therapeutic agents suggested for familial AVMs may be used for sporadic AVMs as well, broadening the scope of patients that can benefit from pharmacological intervention.[71]

Increased endothelial permeability is a hallmark of vascular disease correlated to neo-angiogenesis in injured tissues and congenital malformations such as HHT which is linked to AVM. [35, 65, 72, 73] Loss of function mutations in CCM1 and CCM3 result in upregulation of Vascular Endothelial Growth Factor A (VEGF-A) and VEGF receptor 2 causing an alteration in endothelial permeability in-vitro.[65] Increased VEGF-A/VEGFR enables pathological angiogenesis and may contribute to increased symptomology by increased leakiness of blood vessels in the malformation leading to increased risk of hemorrhage.[65]

Selective loss of CCM2 results in upregulation of Rho kinase which has been linked to loosened junctions and decreased tube formation in endothelial cells in vitro and loss of vascular integrity of endothelial cells in vivo.[74-79] The CCM2 mutation also causes an increase in ADAMTS (a disintegrin and metalloproteinase with thrombospondin motifs) expression which is thought to breakdown a proteoglycan matrix essential in supporting blood vessels, contributing to the development of a cavernoma.[79]

Advancements made in CCM research using gene knockouts may serve as a model for how to approach unexplored avenues in AVM. Genetic analysis may reveal promising groups of genes to silence with the goal of reproducing AVM phenotype.

Conclusion

AVMs are heterogeneous entities that are often found incidentally and treated in acute situations which contributes to the lack of research and consensus on various treatment plans for unique cases. This review has outlined relationships between symptoms and angioarchitecture as well as relationships between treatment options and particular lesion characteristics. Limitations to this review include incomplete retrieval of information. Nevertheless, a holistic exploration of AVM was synthesized by a wide variety of sources to prevent this.

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Experience

Learning with the Community: An Enriching Experience

Shambhavi Chowdhary.[1]

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Introduction

Over the course of time, medicine has undergone great change, shifting its view from the community to the individual. In times when the trend to attain specialty and sub-specialty degrees is on the rise and the healthcare delivery system being converted to a service-provider and customer relationship, health needs of the society as a whole is being sidelined. This is where Community Based Medical Education (CBME) assumes significance. CBME refers to a form of learning wherein medical students understand the principles of basic medicine in a community setting. [1-3] With this perspective in mind, the concept of Village Adoption Scheme (VAS) has been developed in Mahatma Gandhi Institute of Medical Sciences, Sevagramwhich has evolved since its inception in 1969. [4]

First year students of the institute adopt a village where each student is allotted 4-5 families. I too attended the camp and it was my first exposure to community-based learning. We stayed in the village for 15 days in a camp setting and, thereafter, continued with monthly visits for follow-up for the next three years. Combined with better access to health care services for the duration of the camp for the villagers, VAS ensures strengthening of the healthcare delivery system. [5-6]

The fears of those of us, who were new to village life, were soon overcome when we were received with open arms in our families (***Figure 1***). Over the days, as our rapport with our families grew stronger, our focus widened to include certain essential but neglected contributors to health. We gradually started realizing the impact of socio-economic status, environmental and housing conditions, standard of living, on the long-term health of a person. Together with this came a sense of helplessness. Most of the households in rural areas fit a low socioeconomic status. This not only makes affordability and access to health services difficult for them but also affects the social determinants of health. [7] Health improvement in a community cannot be viewed as a task to be accomplished by the health sector alone. Public health demands a more holistic approach. [8-10] Achieving 'health for all' is not possible without engaging 'all for health'.

Certain simple actions like proper hand washing, filtering of drinking water, maintenance of menstrual hygiene, and proper breastfeeding still need attention in the rural areas (***Figure 2***). With a fair understanding of the constraints these families face, we decide objectives for behavior change for each family allotted to us and work towards achieving this over the next three years through various behavior change strategies.[11]

One of the families allotted to me had a well-maintained kitchen garden, which not only supplemented their dietary requirement but also eased their economic burden. I discussed this with my colleagues and they then encouraged their families to also develop kitchen gardens. Solutions to the problems of the community can be found within the community itself, which need to be identified and promoted.

The deeply entrenched ideas of the villagers, coupled with the fact that we were viewed as outsiders, made it difficult to bring about a change. With cooperation from the village school, we set up a meeting with all the village children. That evening, which began with rapport building, went on to become a strong bond of trust and friendship. The health messages that we intended to deliver in the village were first conveyed to these children, who now became our partners. In addition, we were assured, that even after our camp ends, these messages would reverberate within the village.

Apart from children, there are other platforms in form of community-based groups which have the potential to change social norms. These include several self-help groups of women (Mahila Alpa-bachat gath) and a group of adolescent girls (Kishori Panchayat). We interacted with these community-based groups, who hold monthly meetings to discuss numerous issues, including but not limited to health and hygiene. [12-13] These groups also came forward to extend their full support. In their words, they wanted their village to not only be self-sufficient but also empowered and strengthened.

Developing countries such as India still face the problem of inadequate outreach facilities to the peripheral areas for screening, diagnostic and therapeutic facilities. A team from the Department of Community Medicine takes care of the medical needs of the villagers. General and specialist outpatient services, along with medications are provided free of cost during the entire duration of the camp and for the next seven days. Screening facilities provided, include those for anemia, diabetes and hypertension.

This entire stay in our adopted village helped us understand in a small way, the complex web of factors determining health. The present vacuum in medicine demands not only individual skilled physicians, but also proficient doctors able to work in a team, function as effective team leaders and be able to communicate well with patients.

With the white coat comes immense responsibility. It is imperative that we transform our approach to look beyond the walls of the hospital and consider each patient to be a product

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of his lifestyle and living conditions, and not merely a manifestation of disease.

The Village Adoption Scheme, with numerous activities fostering the villager-student partnership coupled with first-hand clinical exposure for first year medical students plays a small but significant role towards the achievement of this goal.14It takes learning beyond the limits of our textbooks and the classroom into the field, where these theoretical principles are turned into hands-on practice. After all, the human body is not just a piece of machinery which can be made to work by fixing a few nuts and bolts. It has also taught me things beyond the medical world and given me precious memories – something that I will hold on to and cherish throughout my life.

Figure 1. A student interacting with family members of one of the families allotted to her. She will continue visiting the family members for the next three years once every month.

Figure 2. Sanitary inspector from Department of Community Medicine demonstrating to the students how to do Chlorination of Well Water.

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The Authors have no conflicts of interest to disclose. Village adoption scheme is one of the curricular innovations at MGIMS, Sevagram, which is being implemented since its inception in 1969 using institutional resources.

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Experience

Integrating Global Health into the Medical Curriculum: Experience of Foreign Students in Ukraine

Victor Ohwo.[1]

Introduction

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (World Health Organization). Medical education consistently focuses on biomedicine despite reliable research and clinical experience showing that the determinants of health are preconceived as social phenomena. [1-4] The medical curriculum of Ukraine is based on the methodology of organizing training processes according to the European Credit Transfer System (ECTS). The curriculum structure is based on 3 cycles of training: humanitarian and socio-economic, natural and scientific, and vocational training. The curriculum incorporates Social Medicine and Hygiene, but course objectives fail to elaborate on qualitative aspects, instead focusing on quantitative elements and Ukrainian Organization of Healthcare.

Global health is a collaborative trans-national research and action for promoting health for all. [5] In total, 19648 international students study health-related courses in Ukraine. (Ukrainian State Center for International Education) Despite this, Global Health is not adequately focused on, especially as majority of these students are citizens of nations with heavy global health burdens. We believe that the medical education curriculum must change to incorporate rigorous training in biosocial health determinants to ensure that all future health professionals are equipped with the knowledge and skills necessary to address complex health problems. For this reason, a 2-day Certificate Course in Global Health for all students in the country was organized.

The course ran from February 8 to 9, 2016. Sessions were held at the Ivano-Frankivsk National Medical University. Registration was done via online forms; the course was mainly promoted for around 20 days, by placing course posters on social media platforms and the university website. Attendees were charged a registration fee of $12 for course materials, meals and logistical expenses. The program involved 11-sessions and was facilitated by Don Eliseo Lucero-Prisno III MD, a professor of Global Health and Public Health at X'ian-Jiantong-Liverpool University, and a renowned Global Health trainer; having previously operated such global health courses in several developing nations all over Asia and Africa. Course Coordinators and the Facilitator created a timetable for relevant topics including: Introductory Lecture on Global Health, Global Health Epidemiology and Global Health Equity, Global Health Economics, Global Health Challenges and Global Health Tools. Student speakers also gave Explanatory lectures. The final session was on Building Careers in Global Health, where the facilitator taught attendees on strategic steps to take in building a sustainable and profitable career in the numerous fields of Global Health. The course was concluded with presentation of certificates of completion for participants.

Certain simple actions like proper hand washing, filtering of drinking water, maintenance of menstrual hygiene, and proper breastfeeding still need attention in the rural areas. With a fair understanding of the constraints these families face, we decide objectives for behavior change for each family allotted to us and work towards achieving this over the next three years through various behavior change strategies. [11]

107 foreign medical students from 12 countries (67% Nigerian, 9% Jordanian, 6% Kenyan, 4% Iraqi, 3% Namibian, Ghanaian and Polish, 1% Indian, Congolese, Pakistani, Zambian and Palestinian) and 7 medical universities all over Ukraine participated in the course. 56% of participants were male, 44% female. 95% of participants were in clinical years of study (4th – 6th years), while 5% were in pre-clinical years (1st – 3rd years). Participants were successfully instructed on the basic theories and concepts including current trends, challenges and debates in Global Health. Attendees completed brief exercises on: **Developing Frameworks in Global Health**, where students were tasked with linking an overt health outcome with all its determinants and consequences, and **Cost-Effectiveness of Global Health Interventions**, where they role-played as health consultants and academics tasked to provide advice to a major funding agency on whether to fund an intervention to control a certain type of infectious disease in a region.

The novelty of such a course in this part of the world, for this group of students, highlighted gaps in knowledge pertaining to Global health. Participants' interests were piqued by the insidious etiologies that underlie many of the diseases they have been taught in class.

The conclusions from this initiative include:

1. There is clear undeniable interest from foreign medical students to know more about the intricacies and determinants of health, especially on the global landscape.
2. The wealth of foreign medical students in Ukraine is an untapped resource, as to the future of global health in developing countries.
3. Integrating global health into the educational curriculum is an assured way to broaden the horizons of upcoming physicians on what it takes to be a 21st century doctor.

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4. Global health lessons can be easily woven into the medical education schedule without being interruptive on other subjects of study.

The aim is to develop a curriculum and make it a mainstay in medical education of foreign students in Ukraine. Several models for integrating social sciences into medical curricula have been described. [6, 7] We believe that efficient integration can be achieved by: building a community of individuals and organizations that acknowledge a broader approach to health, collaborating with curriculum commissions, and establishing institutional backing by emphasizing credible research that demonstrates the importance of Global Health.[8]

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Experience

The Travels of a Volunteer with a Pregnancy Simulator

Kota Hakoyama.[1]

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Introduction

After completing the first three years of basic medicine courses at my medical school, I was determined to take a leave of absence and travel around the world as a "pregnant" man (***Figure 1***). Of course, I was not actually pregnant myself; my plan was to hike across various countries wearing a pregnancy simulator, aiming to encourage males to be more sympathetic to mothers. The pregnancy simulator, filled with 10 kg of water, simulates the weight of a pregnant mother's belly. That is, by wearing it, one can experience one of the hardships that pregnant women face during their last month of pregnancy.

Figure 1. The Author with the Pregnancy Simulator and a Participant in Istanbul, Turkey.

After earning the travel budget by working part-time and using a crowd-funding service, I started the journey from my home country, Japan, in February 2015. In the 468 days that followed, I traveled to 43 countries spanning Asia, the Middle East, Europe, Africa and Latin America. I used local buses and trains to travel inland and stayed in budget accommodation to cut back on spending. Every three days in each country, I hiked with my pregnancy simulator and asked local males to wear it. I considered this project to be of utmost importance for peer education and saw it as indispensable for realizing gender equality. [1]

When I was wearing the simulator over my belly, I feared that someone might mistake me for a suicide bomber. To avoid trouble, I knew that I needed to explain my project with sufficient clarity. Therefore, I first made detailed instructions in each local language, cooperating with bilingual people who could use English. After finishing preparations, I went out into the cities and talked with local people. I thought this would be better as I figured men would prefer to gather in informal settings for social interaction. [2]

Upon beginning this adventure, I would introduce the project's concept and place the simulator on anyone who would accept my invitation to participate. I generally asked participants to do three things; to walk around or climb stairs, to pick up something from the floor, and to lie down. I wanted participants to experience a piece of daily life with the simulator and feel the difference for themselves. After that, I spread my message, saying "please take care of your baby, your wife and your mother. Respect women and be a good father!"

You may wonder why I thought about starting this strange project. I am especially interested in maternal and child health, partly because of my respect for my mother. After my parents divorced, she worked as a high school teacher to bring up her three children, including myself. I vividly remember her words, "we don't have a lot of money, but I will always pay whatever you need to study." Thanks to her generosity, I was able to successfully enter medical school and chase my dream.

The country I achieved the most in during this project was Iran, which I was told is famous for the hospitality of its people. I was determined to visit but remained a bit worried after some friends advised me not to go there because of concerns about unrest in the region. However, when I visited, I found that my anxiety was completely ungrounded. Everyone listened to my story eagerly and said "the Quran, the teaching of Islam, says you must try to best take care of the mothers. From this viewpoint, your project is perfect!" (***Figure 2***). Muslim people said similar statements to me not only in Iran but also in Morocco, Azerbaijan and Sudan. Surprisingly, only Muslim people mentioned religion during the pregnancy simulation, and I realized that I had been judging the people of this region based on stereotypes I had heard that "the Middle East is dangerous". Whenever I became discouraged, I often recalled their kind words to give me the strength to continue my project.

In total, 1070 people tried the pregnancy simulator throughout my project. Generally, 1 in 3 men accepted my invitation to wear the simulator. Most people refused, saying things like "I don't have time," or "I have a stomachache." On the other

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hand, there were excellent reactions from those who tried the simulator. At first, most men seemed shy and were not willing to wear the simulator. But once they did, they smiled, and many took selfies with their smartphones. Outside Europe, the pregnancy simulator was largely unknown beforehand to the general public. Particularly in the developing countries of Asia and Africa, I found that many people were surprised to see and hear about such an idea, and quite a number enjoyed it. I was delighted to have this opportunity to communicate with them using the simulator.

Throughout this experience, it was made obvious to me that I was just one person in this huge world, and as such could not change peoples' perceptions easily. However, I am certain that I was the first person to travel around the world with a pregnancy simulator aiming to spread awareness. The days of trial and error I experienced in the project made me stronger, and I will continue to study and take further strides towards more accessible public health campaigns in the future. I will not give up on making the world better for mothers.

Figure 2. A Participant (Wearing the Pregnancy Simulator) and his Wife in Isfahan, Iran.

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