BJU Int 2021; **127:** 729–741 doi:10.1111/bju.15299

BJUI
BJU International

Original Article

Management of patients who opt for radical prostatectomy during the coronavirus disease 2019 (COVID-19) pandemic: an international accelerated consensus statement

Zafer Tandogdu[1,2], Justin Collins[1], Greg Shaw[1], Jennifer Rohn[2], Bela Koves[3], Ashwin Sachdeva[4], Ahmed Ghazi[5,*], Alexander Haese[6,*], Alex Mottrie[7,*], Anup Kumar[8,*], Ananthakrishnan Sivaraman[9,*], Ashutosh Tewari[10,*], Benjamin Challacombe[11,*], Bernardo Rocco[12,*], Camilo Giedelman[13,*], Christian Wagner[14,*], Craig G. Rogers[15,*], Declan G. Murphy[16,*], Dmitry Pushkar[17,*], Gabriel Ogaya-Pinies[18,*], James Porter[19,*], Kulthe Ramesh Seetharam[20], Markus Graefen[21], Marcelo A. Orvieto[22,*], Marcio Covas Moschovas[20,*], Oscar Schatloff[23,*], Peter Wiklund[10,*], Rafael Coelho[24,*], Rair Valero[25,*], Theo M. de Reijke[26,*], Thomas Ahlering[27,*], Travis Rogers[20,*], Henk G. van der Poel[28,*], Vipul Patel[20,*], Walter Artibani[29,*], Florian Wagenlehner[30], Kris Maes[31], Koon H. Rha[32], Senthil Nathan[1], Truls Erik Bjerklund Johansen[33], Peter Hawkey[34,35] and John Kelly[1,2]

[1]Department of Urology, University College London Hospital, [2]Medical School, University College London, London, UK, [3]Department of Urology, Budapest Hospital, Budapest, Hungary, [4]Department of Urology, NHS Foundation Trust, Freeman Hospital, Newcastle Upon-Tyne, UK, [5]Department of Urology, University of Rochester, Rochester, NY, USA, [6]Leitender Arzt für Roboterassistierte Urologie, Martini-Klinik am UKE GmbH, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, [7]Department of Urology, OLV Hospital, Aalst, Belgium, [8]Department Urology, Robotics and Renal Transplant, Safdarjang Hospital and VMMC, New Delhi, [9]Department of Urology, Apollo Hospitals, Chennai, India, [10]Department of Urology, Icahn School of Medicine at Mount Sinai, New York, NY, USA, [11]Department of Urology, Guy's and St Thomas' Hospitals, London, UK, [12]Department of Urology AOU di MIdena, University of Modena and Reggio Emilia, Modena, Italy, [13]Marly Clinic and the San José Hospital, Bogota, Colombia, [14]Head of Robotic Urology, St. Antonius – Hospital Gronau, Gronau, Germany, [15]Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA, [16]Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Vic., Australia, [17]Urology, MSMSU, Moscow, Russia, [18]Hospital Universitario Rey Juan Carlos, Madrid, Spain, [19]Swedish Medical Center, Seattle, WA, [20]Adventhealth Global Robotics Institute, Celebration, FL, USA, [21]Martini-Klinik, University-Hospital Hamburg-Eppendorf, Hamburg, Germany, [22]Department of Urology, Clinica Alemana, Santiago, [23]Department of Urology, Sudmedica Health, Valparaiso, Chile, [24]University of São Paulo School of Medicine, São Paulo, Brazil, [25]Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA, [26]Department of Urology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [27]University of California, Irvine, Orange, CA, USA, [28]Department of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands, [29]Department of Urology, University of Verona, Verona, Italy, [30]Department of Urology, Pediatric Urology and Andrology, Justus-Liebig-University, Giessen, Germany, [31]Hospital Da Luz, Lisbon, Protugal, [32]Department of Urology, Institute of Urological Science, Yonsei University, Seoul, Korea, [33]Department of Urology, Institute of Clinical Medicine, University of Oslo, Oslo, Norway, [34]Institute of Microbiology and Infection, University of Birmingham, Birmingham, and [35]Queen Elizabeth Hospital Birmingham, Birmingham, UK

*Delphi working group.

Objective

Coronavirus disease-19 (COVID-19) pandemic caused delays in definitive treatment of patients with prostate cancer. Beyond the immediate delay a backlog for future patients is expected. The objective of this work is to develop guidance on criteria for prioritisation of surgery and reconfiguring management pathways for patients with non-metastatic prostate cancer who opt for surgical treatment. A second aim was to identify the infection prevention and control (IPC) measures to achieve a low likelihood of coronavirus disease 2019 (COVID-19) hazard if radical prostatectomy (RP) was to be carried out during the outbreak and whilst the disease is endemic.

Methods

We conducted an accelerated consensus process and systematic review of the evidence on COVID-19 and reviewed international guidance on prostate cancer. These were presented to an international prostate cancer expert panel (n = 34)

through an online meeting. The consensus process underwent three rounds of survey in total. Additions to the second- and third-round surveys were formulated based on the answers and comments from the previous rounds. The Consensus opinion was defined as ≥80% agreement and this was used to reconfigure the prostate cancer pathways.

Results

Evidence on the delayed management of patients with prostate cancer is scarce. There was 100% agreement that prostate cancer pathways should be reconfigured and measures developed to prevent nosocomial COVID-19 for patients treated surgically. Consensus was reached on prioritisation criteria of patients for surgery and management pathways for those who have delayed treatment. IPC measures to achieve a low likelihood of nosocomial COVID-19 were coined as 'COVID-19 cold' sites.

Conclusion

Reconfiguring management pathways for patients with prostate cancer is recommended if significant delay (>3–6 months) in surgical management is unavoidable. The mapped pathways provide guidance for such patients. The IPC processes proposed provide a framework for providing RP within an environment with low COVID-19 risk during the outbreak or when the disease remains endemic. The broader concepts could be adapted to other indications beyond prostate cancer surgery.

Keywords

pandemic, consensus, nosocomial, coronavirus, surgery, #PCSM, #ProstateCancer, #uroonc, #COVID19, #Coronavirus

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has affected healthcare at multiple levels with inevitable delays in provision of care for patients with other conditions, such as cancer. This includes men with non-metastatic prostate cancer who are awaiting surgical treatment [1,2]. Prostate cancer is a heterogenous disease, with a global annual incidence of 1.3 million and 419 000 deaths per annum [3]. Non-metastatic prostate cancer is categorised into three main risk groups (low, intermediate and high) based on risk of disease progression [4,5]. Radical treatment, including surgery or radiotherapy (RT), mostly benefits men with intermediate- or high-risk disease with a life-expectancy of >10 years [5]. Prolonged delay in treatment will probably result in disease progression with consequent loss of ability to preserve periprostatic structures impacting on functional outcomes. Furthermore, the expected duration of delays to curative treatment remains unclear, but any delay will result in a backlog in the number of men awaiting radical treatment. Delays to the diagnostic pathway from PSA testing to biopsy will also add to the backlog and result in later presentation of more advanced disease, which poses a risk to patient wellbeing. Mitigation of these risks during the COVID-19 pandemic necessitates reconfiguration of management pathways and development of strategies to prioritise patients. An additional challenge is the need to protect both patients and healthcare workers from contracting COVID-19 until the disease is either eradicated or vaccines are developed, whilst ensuring the safe delivery of radical treatment for those in need.

The first aim of the present study was to develop guidance on reconfiguring the management pathways for patients with prostate cancer with non-metastatic disease whose radical surgical treatment is delayed due to the COVID-19 outbreak. A second aim was to identify the basic requirements of achieving low likelihood of COVID-19 hazard within a healthcare unit intending to offer prostate cancer surgery, whilst the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains in the population (a so-called 'COVID-19 cold' site). We used an accelerated consensus by adapting the Delphi methodology to provide guidance in the absence of substantial evidence during the COVID-19 outbreak. In addition, we hope that the infection prevention and control (IPC) principles will be of relevance for other specialties planning to deliver surgery as long as COVID-19 remains in the community without definitive treatments or vaccines.

Materials and Methods

The study consisted of three objectives where each phase informed the subsequent phase. First, a systematic review of the literature and current published guidelines was completed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [6]. Second, the systematic review informed a series of questions from which answers by consensus were sought. Third, the obtained consensus, in turn, helped map a pathway for the reconfiguration of prostate cancer management for patients who opt for surgery if a backlog develops during the COVID-19 outbreak and establish the components for how to deliver surgery whilst COVID-19 can spread in the community.

Evidence Synthesis: COVID-19 and Prostate Cancer

The first teleconference was conducted on Saturday 4 April 2020 and the second on Tuesday 7 April 2020. At the inception of this project there was limited evidence published for COVID-19 and its impact on surgery. The available evidence was used to develop questionnaires for the Delphi consensus process. This process was carried out by authors with expertise in infectious diseases (Z.T., P.H., J.R., T.E.B.J., F.W., B.K.). A systematic review of the literature was carried out using the Medical Literature Analysis and Retrieval System Online (MEDLINE; accessed from PubMed to identify published articles from 1 January 2020 to 30 March 2020; further details are supplied in Appendix S1). Guidelines and recommendations regarding COVID-19 published by WHO, Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC), and National Institute for Health and Clinical Excellence (NICE), were reviewed. Publications identified from reference lists of these documents were also reviewed.

The aim of this evidence synthesis work was to identify questions relevant to:

1. Frequency of asymptomatic patients with COVID-19.
2. Incubation period of COVID-19.
3. Sensitivity and specificity of available diagnostic tests for COVID-19 in asymptomatic patients.
4. Stages of contagiousness.
5. Duration of contagiousness.
6. Risk factors for severe outcomes in patients who develop COVID-19.
7. In-hospital IPC measures that can be implemented to establish an environment protective for both the patient and healthcare workforce before, during, and after RP.
8. Prostate cancer management guidelines, to review existing pathways and suggest modification in order to minimise risk during the pandemic (Appendix S2).

The prostate cancer guidelines and recommendations published by the European Association of Urology (EAU) and National Comprehensive Cancer Network (NCCN) were reviewed (Z.T., J.C., G.S.). Information summarised by these documents was used to establish the baseline of current expected practice for patients with prostate cancer who are eligible for radical treatment.

Expert Panel Teleconference Meeting

An advisory panel was formed that was comprised of key opinion leaders with a specialist expertise in infectious diseases, prostate cancer management and/or robotic surgery programmes (Appendix S3). J.K., P.H., J.C. and Z.T. chaired panels. In total 38 experts from four continents including seven countries from Europe (Belgium, Germany, Hungary, Italy, Netherlands, Norway, UK) were brought together to discuss and develop an international standard for the development of a cold site for managing prostate cancer during the pandemic. At the time of the consensus, Europe was at the centre of the pandemic and experts were selected from countries with different healthcare contexts to allow generalisability of findings. Experts with recent experience in managing patients with prostate cancer during the COVID-19 crisis were included (Italy/Spain/New York/California). A total of 36 panel members were qualified as surgeons (including four members of the EAU section of Infections in Urology, for which three have expertise in nosocomial infections) and two were experts on infection prevention and control as well as virology (see Appendix S3 for composition of the panel and roles). The teleconference meetings comprised presentations (Appendix S4) on the subject matter, clarifications of current evidence, and reviews of the literature findings. Overviews of the various strategies for the development of COVID-19 cold sites were discussed.

Internet Survey and Consensus Process

Following the teleconference, the consensus process was conducted amongst the experts. An internet survey (Google forms) was generated and sent to the 34 members of the panel (Appendix S5). An accelerated e-consensus-reaching exercise, over 3 consecutive days, by using the Delphi methodology, was then applied [7]. The Delphi method structures group communications so that the process is effective in allowing a group of individuals to deal with a complex problem. We consented participants prior to the process and its time points. This was particularly important in accelerating the process.

Questions in which there was ≥80% consensus were removed from the next round of the survey. Repeated iterations of anonymous voting continued over three rounds, where an individual's vote in the next round was informed by knowledge of the entire group's results in the previous round. To be included in the final recommendations each survey item had to have reached group consensus (≥80% agreement) by the end of the three survey rounds. In the Delphi process the finding of 'consensus' is more relevant than the level of consensus. Levels of consensus are reported in Appendix S5.

The process applied adhered to the principles of Delphi methodology of, (i) selection of panel members – experts, (ii) development and application of questions in rounds, (iii) evolution of responses, and (iv) divergence towards a consensus [7]. Although the implementation of a Delphi process can be variable, the strict time frames we applied are novel. Therefore, we have coined the process as a 'consensus statement'.

Pathway Development

The purpose of the pathway development and mapping is to systematically assemble evidence to provide guidance for clinicians. The existing pathways were reviewed and reconfigured using available evidence, published similar pathways, and input from the consensus process [4,5,8]. Subsequent to the consensus process, plausible scenarios to plan for delays in radical surgical treatment from the point of risk stratification of prostate cancer onwards were illustrated in a one-page comprehensive flow chart. This was an iterative process whereby the consensus panel was consulted to review the prepared pathway until agreement was reached.

Findings

Evidence and Guidance for COVID-19

The evidence acquisition process included 2430 records reviewed and 30 full texts were used (Fig. 1). Further studies and recommendations were obtained from the WHO, CDC, ECDC and NICE. Findings are provided in Appendix S1.

Consensus Process

Consensus was reached on multiple items (84.3%, 75/89). Results of the three rounds are summarised in Fig. 2, and details are provided in Appendix S5. The main statements of the consensus process are summarised in Table 1. A detailed summary of the statements is provided in Appendix S6.

Delivery of Surgery

The panel reached consensus on multiple items that collectively contribute to re-arranging a hospital site to deliver radical prostate surgery within a COVID-19 protected environment. These are summarised in Table 1 and the panel agreed to define such sites that adhere to the principles as 'COVID-19 cold'. The panel reached consensus that resource allocation to COVID-19 cold sites should be guided by the resource requirement of COVID-19 patients in individual regions and countries.

Principles of patient flow prior, during, and after surgery are dependent on the sensitivity and specificity of COVID-19 diagnostic tests, as well as the time taken to obtain results. At the time of manuscript preparation there remained a paucity of rapid tests with a high sensitivity and specificity. Therefore, the panel agreed on a set of basic principles and assumptions to be used to keep the risk of COVID-19 as low as possible within the COVID-19 cold sites. The principles that were agreed on include: accounting for the incubation period of COVID-19, the need to operate on patients with minimal risk of contagiousness, and isolation of patients after surgery until catheter is removed (on average 10 days). The panel could not reach consensus on how to implement the preoperative process to ensure that surgery is performed on patients with the least likelihood of contagiousness. Based on the discussions and the reviewed literature the scenarios discussed are illustrated in Fig. 2.

Rationing Prostate Cancer Surgery

The Panel reached consensus on rationing patients with prostate cancer using the EAU risk-classification tool, age, and risk factors for COVID-19 worse outcomes. Statements agreed are provided in Table 1. A conceptual summary of the agreed principles is summarised in Fig. 3.

Reconfiguration of Management Pathways

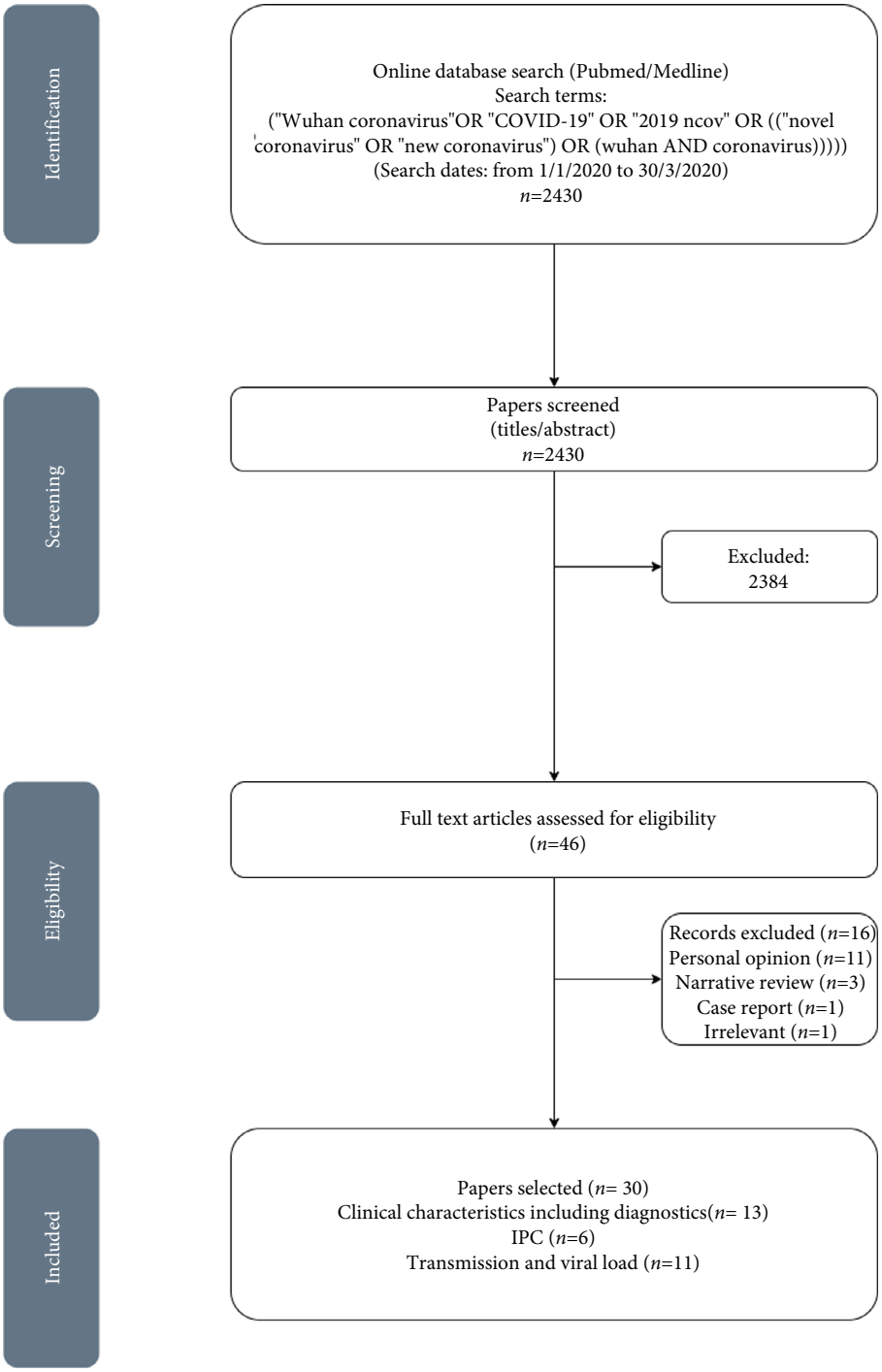
Consensus was achieved to rearrange pathways for patients whose definitive treatment will be postponed using the EAU risk stratification. A conceptual pathway that was mapped based on the panel consensus, and is provided in Fig. 4 with details of statements in Table 1.

Discussion

In the present study an international expert panel developed consensus statements to reconfigure surgical pathways if there was a delay due to the impact of the COVID-19 outbreak. This challenging task was achieved through an accelerated consensus process. The statements were developed with the intention to be utilised as part of a comprehensive response to maintain essential healthcare services, while simultaneously ensuring care for acutely ill patients with COVID-19. The ability of a country to maintain essential healthcare services will be influenced by its underlying resources, incidence of COVID-19 and other cases. Therefore, the consensus was developed to address re-organisation of the pathways for patients with prostate cancer who opt for surgery until healthcare systems resume routine services. In addition, throughout the outbreak there will be variability in the strategic allocation of resources dependent on the incidence of COVID-19. The panel agreed to ration cases for surgery and the underlying concepts to achieve this in a protected environment that minimises risk to the patient and healthcare staff to additional adverse outcomes of COVID-19. These will be helpful for countries that can allocate resources for cancer surgery during the different stages of the pandemic. Beyond this the rationing strategy for prostate surgery cancer will remain relevant once the pandemic is over in prioritising patients within the backlog.

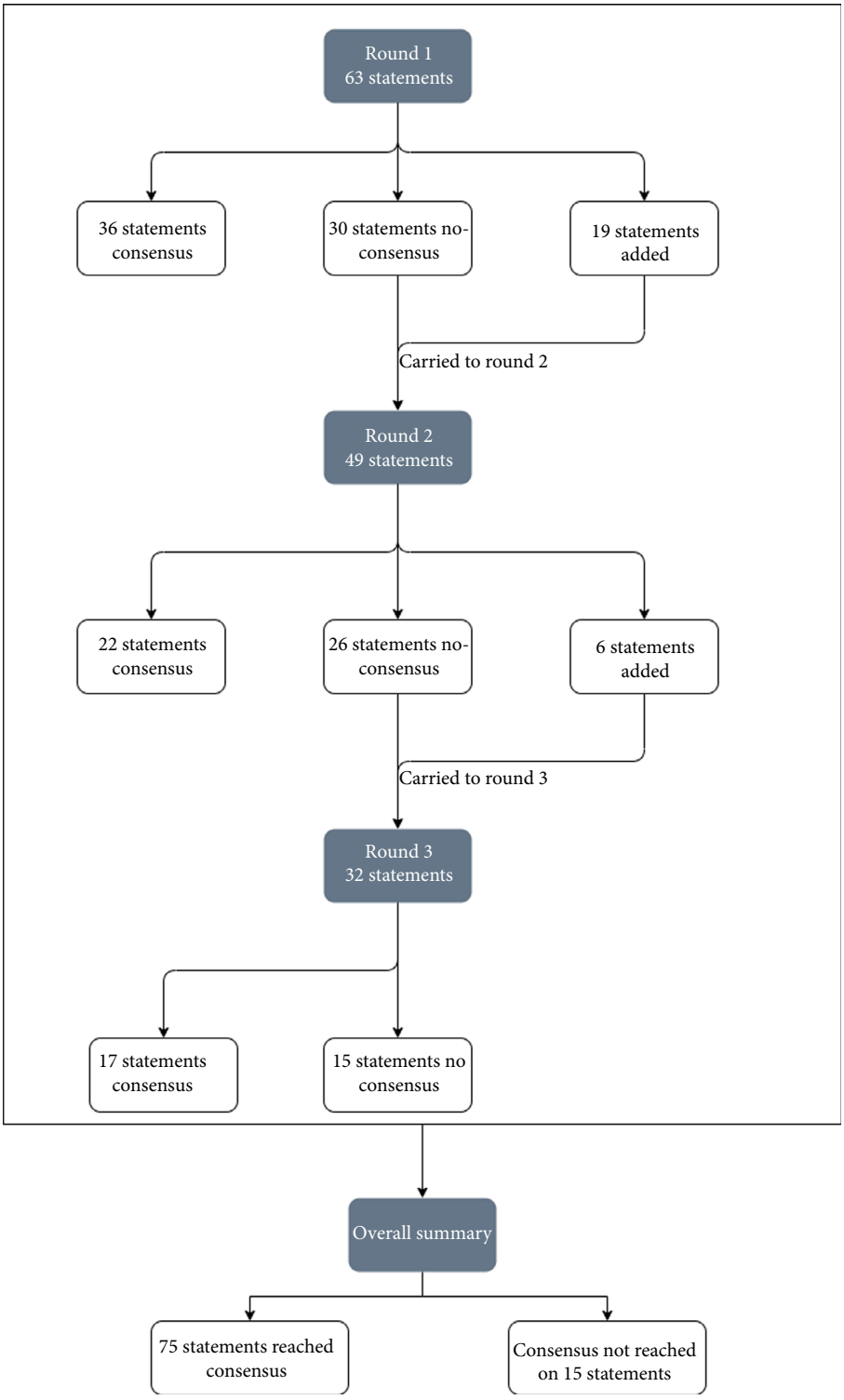
We reached consensus on multiple items related to delivery of surgery and postoperative care, if possible, during the outbreak. Two key concepts that were agreed largely shape

Fig. 1 Flow chart of the published literature review to develop the consensus questionnaire. In addition, recommendations from the WHO, CDC, ECDC and NICE were also reviewed in developing the questionnaire.



the remaining statements of the consensus for delivery of surgery. The first concept is to simultaneously ensure safety of the patient and healthcare staff regarding COVID-19 (i.e. prevention and control of nosocomial COVID-19). The second concept is to assume that at any given time point a patient or healthcare professional can be contagious. Lack of rapid and accurate diagnostics shaped these concepts. This means that at the point of entry to a COVID-19 cold site it is not possible to distinguish if individuals are contagious or not. Viral RNA detection methods can identify individuals

Fig. 2 Summary of the consensus process.



shedding the virus, but this does not necessarily indicate contagiousness [9]. Lack of reliable serology tests and unknown duration of contagiousness after COVID-19 are additional complexities that the panel considered. Nosocomial infections of SARS-CoV-2 within a COVID-19 cold site delivering elective prostate cancer surgery could result in

Table 1 Consensus view on re-organisation of management pathways for patients with prostate cancer eligible for surgical treatment during the COVID-19 pandemic.

COVID-19 pandemic impact on patients with prostate cancer

1. Disruption in healthcare services for patients with prostate cancer
2. Immediate delay in curative management
3. Increase in backlog resulting in subsequent delays
4. Overall increase in likelihood of disease progression

Basic requirements for a unit to deliver prostate cancer surgery whilst sustaining low risk of COVID-19 transmission and consequences

1. Capacity to screen for COVID-19
2. IPC protocols adapted for COVID-19 to be applied for patients
3. IPCs adapted for COVID-19 to be applied by the healthcare workforce
4. Rearrangements of the hospital space and workflow that aims to create and maintain areas with low likelihood of COVID-19 transmission hazard
5. Protocols for rapid isolation of COVID-19-suspected cases detected in the unit into areas separate from COVID-19-free wards
6. Areas with COVID-19-suspected or -confirmed patients that are separate from the prostate cancer screening, treatment and follow-up areas
7. Utilisation of telemedicine whenever possible to ensure good communication and planning whilst minimising hospital admissions

The seven items above collectively contribute to decreasing the risk of COVID-19 transmission (likelihood of hazard) and its consequences (severity of hazard) within a site that delivers prostate cancer surgery. We define such a site as a 'COVID-19 cold' site

Resource allocation for COVID-19-free prostate cancer surgical units

1. In accordance with local resource allocation required for patients with COVID-19
2. Guided by COVID-19 local epidemiology, overall hospital capacity and its estimated future capacity

COVID-19 considerations for patients planned for surgery

Shortly before surgery

1. Patient should be screened for contagiousness of COVID-19
2. Application of optimal general hygienic measures (i.e. hand disinfection)
3. Account for the lag period between becoming contagious and testing positive for COVID-19 and the potential for false-negative tests*
4. If possible, consider self-isolation of asymptomatic patient before surgery, ideally at a location designated by the hospital whereby the patient flow is reviewed and monitored‡
5. Avoid public transportation

Surgery

1. Patient should be non-contagious for COVID-19
2. Consent the patient for COVID-19-related risks and hazards

After surgery

1. Self-isolate at home after discharge at least until indwelling urinary catheter is removed safely (including travel to and from hospital)
2. Do not routinely screen for COVID-19 before discharge if asymptomatic

COVID-19 considerations for the healthcare workforce that will deliver prostate cancer surgery treatment in COVID-19 cold sites

1. Symptomatic healthcare workers should self-isolate and should not attend COVID-19 cold sites
2. Asymptomatic healthcare workers should be screened and reviewed for COVID-19 before a shift†
3. Evidence for the optimal screening method is unclear (symptoms vs viral load vs serology vs imaging)*
4. Liaise with local IPC teams to identify the optimal screening protocol applicable to your region
5. Follow future evidence for antibody screening as a tool to establish risk for healthcare worker (an ideal workforce may be one that has acquired immunity to COVID-19)

PPE

1. Assume that all patients and healthcare workers may be contagious until definitive screening tests are available
2. Use PPE during clinical tasks involving face-to-face contact with patients
3. Level and composition of PPE to be agreed by local IPC teams for each task (i.e. ward rounds, change of catheter, surgery)
4. Evidence is evolving and an adaptive approach should be implemented
5. Consider rational use of PPE due to perceived shortages in supply [8]

Workflow

1. Change the working schedule to ensure safe delivery of service to patients
2. Adapt the working schedule to minimise risk of staff contracting COVID-19 outside the workspace
3. Consider developing weekly shifts where staff is isolated and accommodated on site for the full duration of their shift (the longer the shifts the better for working/screening time ratio)

Theatre space

1. Decrease number of people in theatre
2. Do not allow observers
3. Keep training activity to a minimum
4. If robotic surgery is utilised and local regulations permit, consider placing the console outside the theatre to decrease PPE consumption and traffic in theatre
5. Consider additional measures to minimise risk according to type of surgery and exposure to types of bodily fluids, aerosols, droplets, and surgical plume
6. Consider separate anaesthetic room for intubating and extubating patients, to decrease likelihood of infective aerosol (respiratory) dispersal

Table 1 (continued)

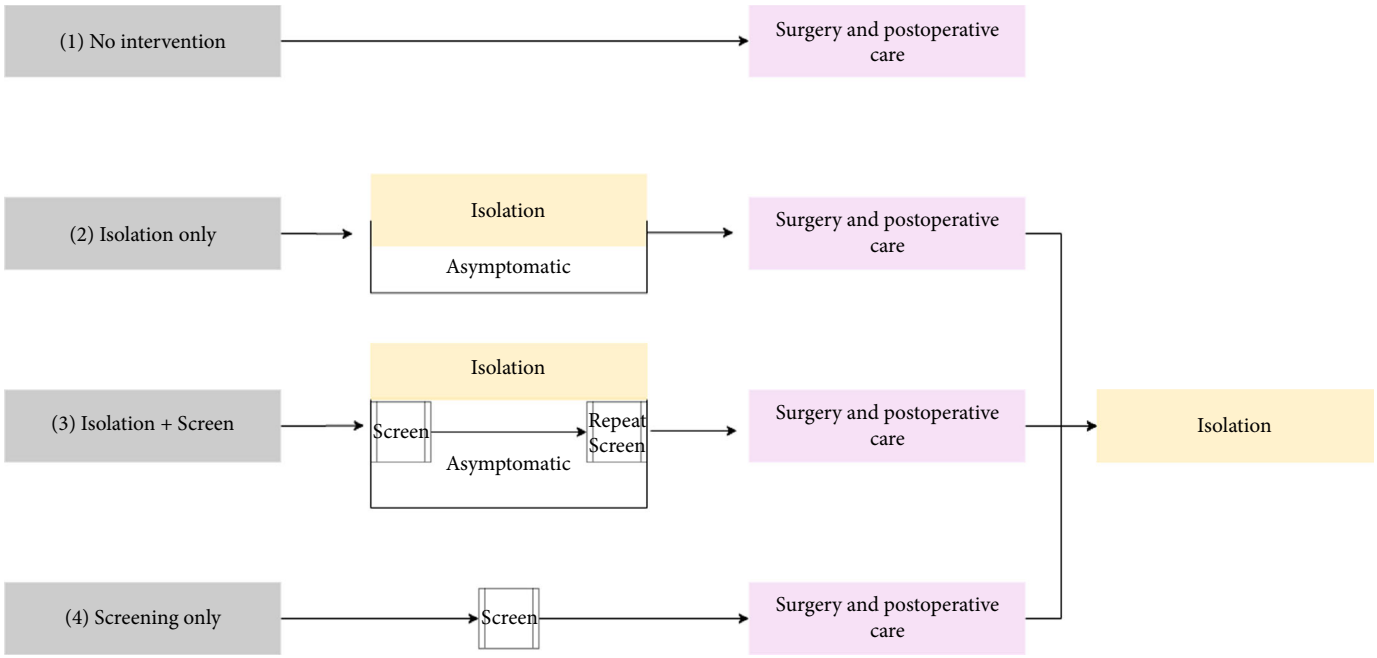
	4. Consider commuting to work in private vehicle where possible or accommodate locally	7. Consider a safety protocol in adherence with local IPC guidance for handling of PPE and other utensils after use
Criteria to use for rationing and prioritisation of management of patients with non-metastatic prostate cancer		
Prostate cancer risk stratification		**Patient risk factors for worse outcomes of COVID-19**
1. Use the EAU risk-stratification tool 2. For intermediate-risk, if needed apply the NCCN criteria for further rationing of patients with unfavourable-risk features 3. For high risk if needed apply the NCCN criteria for further rationing of patients with very-high-risk features 4. The same criteria are applicable for rationing management of patients planned for salvage surgical treatment		1. If a patient is prioritised to receive surgery based on cancer features, further prioritise with COVID-19 risk factors (medical conditions related with COVID-19 adverse outcomes; Appendix S1) 2. If patient is prioritised based on cancer features, further prioritise younger men to receive surgery 3. Prioritise, predicted straight forward cases (i.e. no previous abdominal surgery, obesity, TURP)
Prostate cancer risk groups and relevant management in case of significant delay (>3–6 months) of curative treatment		
Low risk	AS do not offer surgery during the pandemic even if patient is keen for surgery	
Intermediate risk	1. Do not offer androgen receptor blockers for patients whose treatment has been deferred unless there is doubt surrounding diagnostic accuracy/upgrading or upstaging 2. Arrange first follow-up appointment in 3 months 3. Use PSA for follow-up 4. DRE and TRUS not advised for follow-up during pandemic 5. MRI may be used (if capacity allows) in select cases where PSA kinetics and cancer characteristics cause concern	
High risk	1. If possible, offer surgery on the basis of risk of disease progression 2. Consider duration of anticipated delay in surgical treatment prior to commencing LHRH analogues 3. If ADT planned offer LHRH analogues and if not preferred consider bicalutamide 150 mg 4. Arrange first follow-up appointment in 3 months 5. Use PSA and MRI for follow-up: PSA after 3 months and unless concerning PSA kinetics MRI after 6 months (if capacity allows) 6. DRE, TRUS and bone scan are not advised for routine follow-up	
Consideration of pelvic lymph node dissection (PLND) for patients offered surgery		
1. The balance of survival benefit and harms of extended PLND (ePLND) for intermediate- and high-risk disease are unclear 2. An ePLND provides improved clinical staging for intermediate- and high-risk disease 3. For high-risk patients adhere to the decision-making process to which you normally adhered to before the COVID-19 pandemic, whilst taking care to avoid inherent risk of complications		
Post-surgical follow-up protocols		
1. Aim at keeping hospital visits to a safe minimum 2. Arrange first postoperative PSA check at 3 months 3. Where possible (i.e. no perioperative complications and uneventful catheter removal), use telemedicine for clinical consultations		

**At the time of the consensus and writing the manuscript no screening approach based on either a single or combination of tests has been found to offer <5% false-negative rate. Testing location (out of hospital vs in hospital) process is also unclear. †Rearrangement of the working hours of the healthcare workforce is intended to reduce the likelihood of getting infected with COVID-19 outside the COVID-19-free hospitals. ‡Isolation strategy is unclear. Possible options are to isolate for 2 weeks before surgery at home and ensure isolated travel to hospital. Lack of evidence at multiple levels prevented the panel from giving specific advice, but the concept for isolation was agreed.*

serious consequences and defeat the purpose of such a site. Initial series indicate that in COVID-19 treatment sites the nosocomial infection rate could be up to 41% [10]. Concepts adopted by the panel can be considered as a safe option that maintains the COVID-19 cold site functional throughout the outbreak until SARS-CoV-2 is either eradicated from community or a vaccine is developed. However, these concepts generate significant operational challenges including reconfiguration of the work and patient flow and utilisation of large amounts of personal protective equipment (PPE).

Concerns of inadequate global PPE stockpiles mean that effective and appropriate use of PPE is imperative to maintain safe healthcare provision as long as COVID-19 remains in the community [11]. Adjustment of PPE composition based on likelihood of contagiousness was successful during the 2015 Middle Eastern Respiratory Syndrome outbreak and similar approaches can be adopted for COVID-19 cold sites to ensure efficient use of PPE [12]. Due to absence of definitive diagnostics, a combination of measures can be utilised to decrease the likelihood of COVID-19 contagiousness of an individual and guide PPE use. A key strategy can be isolation of the patient prior to surgery in combination with diagnostics (summarised in Fig. 2 and Appendix S7). We failed to reach consensus on

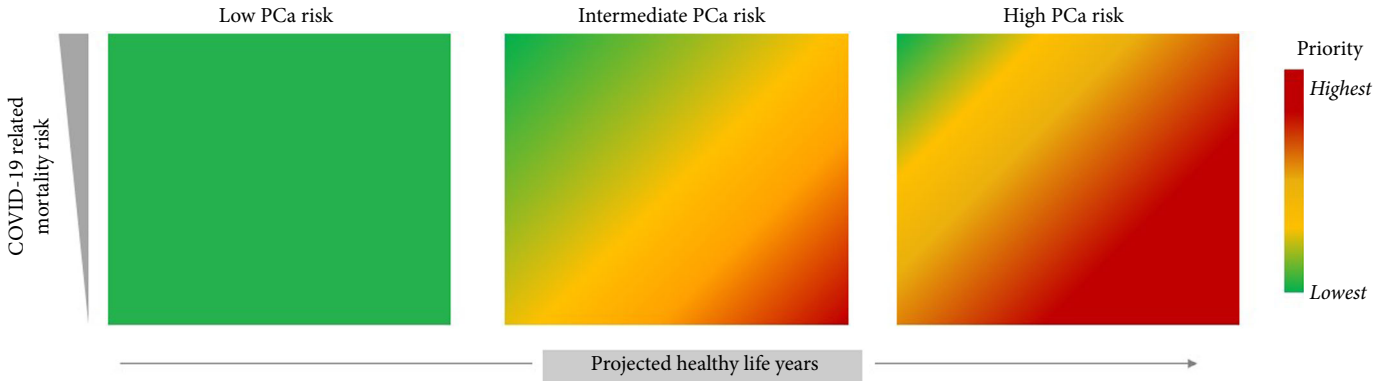
Fig. 3 Protocols for prevention of COVID-19 before, during, and after surgery. (1) No intervention: The patient flow followed before the COVID-19 outbreak. This flow does not reduce the risk of operating on COVID-19(+) patients. It exposes the patient, healthcare professionals and other patients on wards to increased risk of COVID-19. The panel advised against operating on patients with a high likelihood of COVID-19. This scenario would be the most PPE-exhaustive approach. (2) Isolation only: In this protocol the patient is kept under isolation for a set period of time that would ideally cover the incubation period of COVID-19. If patient remains asymptomatic throughout isolation, they can be assumed to be at low risk of COVID-19. Implementation of this strategy should account for logistics such as self-isolation vs isolation at a designated site selected by the COVID-19 cold hospitals. The success of this strategy relies on strict isolation and ideally should cover 14 days (97.5% of patients' incubation period). (3) Isolation and screening protocol: In this protocol the patient is screened for viral RNA at the beginning and the end of the isolation period. It could be helpful in different ways. First, it can reduce the duration of the isolation period (i.e. double swab negative within 48 h low likelihood of COVID-19 carrier). Second, if a long isolation is suggested (i.e. 2 weeks) the first screen can be considered as a safety check at entrance of self-isolation. Thus, if a patient is positive on first screen that means their surgery should be postponed; therefore, useful in scheduling for theatres. The 2-week isolation with double swabs at entrance and exit of isolation is the safest option until the self-isolation compliance can be secured that negates the exit swab. See Appendix S6 for different strategies on implementing this approach. (4) Screening only: This protocol assumes utilisation of a rapid diagnostic test that informs the clinicians regarding COVID-19 contagiousness and immunity status of individuals. Protocols 2–4 assume that the COVID-19 outbreak is ongoing and therefore suggests that patient self-isolates after discharge until removal of indwelling urinary catheter (consensus by panel).



isolating patients for 48 h in a designated room (external to but near the hospital) and screening the surgical candidate at entry and end of isolation. At the final consensus meeting, it became apparent that panel members who rejected this statement were concerned that infrastructure to deliver this was not available at their own site. Current knowledge indicates that the incubation period on average is 5 days, but this can extend up to 14 days [13]. Therefore, the safest duration of preoperative isolation would be 14 days. This could be combined with an RNA-viral test at the beginning and end of isolation if resources allowed. Isolation of patients can be carried out in single isolation rooms or cohort rooms based on IPC guidance [14]. Our panel also suggested that countries that cannot provide the required resources for patients to isolate in hospital before surgery should instead, advise patients to self-isolate at home. Countries will need to adapt these recommendations to what is achievable within their means. The success of self-isolation at home before surgery relies on the compliance of patients. To improve compliance to quarantine of suspected cases Taiwan utilised mobile tracking technology to monitor patient movements [15]. Interventions to improve compliance to self-isolation at home before surgery will be a challenge that needs to be addressed uniquely for each country and culture. Overall, the success of a COVID-19 cold site will be dependent on the applied process, hospital resources, efficient use of PPE, and compliance with the recommendations that are regularly updated as new evidence emerges. Finally, the panel provided a set of recommendations to decrease PPE consumption during surgery, such as placing the robotic surgical console in a separate room and utilising telemedicine as suggest by the WHO [11,16]. This would be subject to local regulations.

Reconfiguration of patient and healthcare staff flow is a vital IPC measure to achieve and protect a COVID-19 cold site. A hospital in Sichuan, China, applied rigorous IPC measures

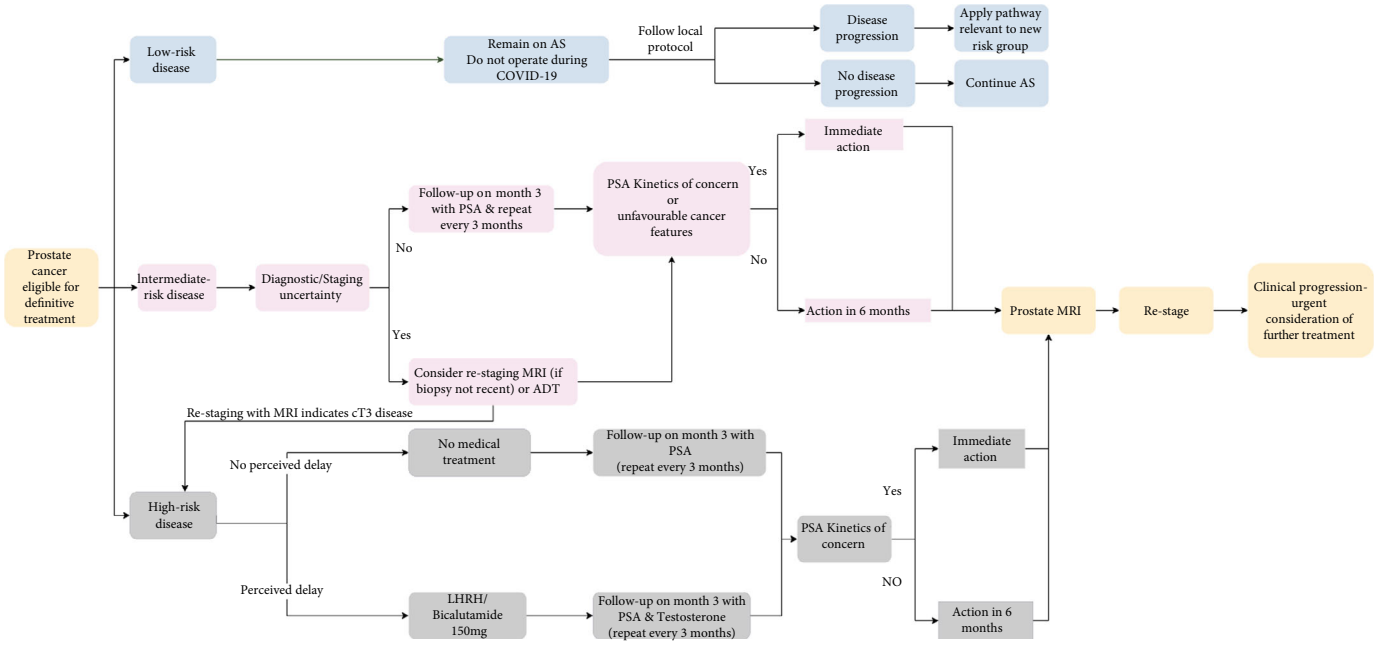
Fig. 4 Conceptual pathway for patients with prostate cancer whose definitive treatment will be delayed.



including reconfiguration of flow within an emergency radiology department, succeeding in protecting all healthcare staff from COVID-19 despite carrying out 3340 CT scans on COVID-19 suspected cases within 47 days [17]. Our panel agreed to take further measures to control staff flow, such as changing working shifts to a week or beyond and reside at the hospital site. It is expected that this can help in effective resource allocation by negating the need for frequent screening of healthcare staff and reduce risk of transmission of COVID-19.

Decrease in available resources to maintain essential healthcare services, limited PPE supply, and risk of COVID-19 adverse outcomes in the general population have created the urgent need to ration prostate cancer surgery [11,18]. We agreed that the decision to offer prostate cancer surgery during the pandemic should be made by weighing up the risk of prostate cancer disease progression and the risk of COVID-19 adverse effects (Fig. 4). Of note, it is currently unclear whether surgery during the pandemic increases the risk of mortality from COVID-19. Although a recent paper based upon a small heterogenous cohort of COVID-19 confirmed cases undergoing elective surgery at an early time point during the current pandemic has indicated that this could be the case [19]; however, selection bias within this cohort limits our ability to refute or support this hypothesis. Nevertheless, patients who developed severe COVID-19 features within this surgical cohort tended to be older patients with one or more comorbidities. Our proposed approach to select patients for prostate cancer surgery during the pandemic prioritises younger patients with

Fig. 5 A conceptual illustration of surgical prioritisation process of patients with prostate cancer during the COVID-19 pandemic. PCa, prostate cancer.



higher-risk disease with only one or zero comorbidities (Fig. 5).

Prostate cancer risk stratification was considered to play a crucial role in selecting patients most likely to benefit from surgery during the pandemic. The panel agreed that patients with low-risk disease should be placed on active surveillance (AS) protocols, irrespective of their preference for immediate surgery. This is supported by findings from e.g. the Prostate Cancer Intervention Versus Observation Trial (PIVOT; ClinicalTrials.gov Identifier: NCT00007644) reporting only minor survival benefit amongst patients with low-risk disease treated with surgery [20]. We agreed that NCCN criteria can be used to further subgroup the intermediate-risk patients and AS can be offered to the favourable group per results from the Prostate Testing for Cancer and Treatment trial (ProtecT; ClinicalTrials.gov Identifier: NCT02044172) [21] and observational data [4,22]. Furthermore, inaccurate initial disease staging is known to result in subsequent upstaging in ~30% patients with intermediate-risk disease [23]. Beyond that there is concern that untargeted biopsies and absence of MRI scans for staging can miss extraprostatic extension [24]. Thus, the panel agreed upon closer surveillance of conservatively managed intermediate-risk patients, with repeat staging with MRI at 6 months, if available. The proposed pathway advises that patients upstaged at this point should be offered immediate definitive treatment or androgen-deprivation therapy (ADT), after weighing up the risk of COVID-19 adverse effects.

Patients with non-metastatic high-risk prostate cancer may be managed by either immediate surgery in the absence of COVID-19 risk features, or alternatively offered ADT until safe to proceed to surgery, although this will have a considerable impact on the patients' quality of life. Previous observational studies have shown that it may be safe to defer surgery in high-risk disease by up to 90 days with the use of ADT [25]. However, recent modelling estimates have predicted that the COVID-19 pandemic may continue for >3 months and possibly until a vaccine is developed [26], which is likely to delay treatment for a subset of older patients with high-risk prostate cancer and multiple comorbidities. Based upon data from the control arm of the Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy trial (STAMPEDE; ClinicalTrials.gov Identifier: NCT00268476), it is anticipated that 32% of patients with N0 and 47% of patients with N1 disease within this ADT cohort are likely to progress over a 2-year period [27]. In addition, long-term ADT should be avoided in patients with multiple pre-existing comorbidities due to risk of developing additional comorbidities [28].

External beam RT (EBRT) can also be considered for men with prostate cancer [5]. During the pandemic, this option would possibly have limited use as it requires multiple and frequent hospital visits (total 20–25 hospital visits within 4–5 weeks) increasing the risk of COVID-19 for the patient [5]. The EAU guidelines rapid response group suggested postponing RP until the end of the pandemic, whilst proposing that EBRT can still be offered [29]. They also suggested keeping outpatient visits as low as possible, which contradicts with the offering of RT during the pandemic. With the introduction of COVID-19 cold sites the heterogeneous epidemiology of the pandemic is taken into account and the multiple risks accompanying can be mitigated and provide surgery as an option for patients if necessary.

Our approach to employ a consensus process was particularly helpful in accomplishing our objectives. The Delphi process is useful for complex issues that cannot be subject to clinical studies. For such circumstances they are impactful and help in standardising management. The COVID-19 outbreak has created circumstances with great uncertainty that reflected on to urological practice [30]. For instance, an online survey identified that in 13% of urology practices urologists were encouraged by their managers not to wear face masks [30]. The time sensitive issues meant that we had to apply an accelerated process to achieve our objectives. In our present study, we adhered to the fundamental principles of a Delphi consensus process [7]. The methodology does not dictate the duration of the process, but due to the nature of urgency and scale of the events we applied an accelerated process. To our knowledge this is a novel approach that has not been published before. This was time intensive and to achieve success all participants were consented prior to entering the study to adhere to the strict time schedule. The process also required similar consent for the questionnaire development by experts in infectious diseases (P.H., J.R.), nosocomial infections in urology (Z.T., T.E.B.J., F.W.) and prostate cancer surgical management (G.S., J.C., J.K.). The accelerated consensus we carried out by adhering to the principles of Delphi methodology is novel and we refer to it as a 'consensus statement'. Despite the strengths of the work there are some caveats. Firstly, the panel members were from 16 different countries around the world, but most were from Europe and the USA. We therefore concentrated on establishing the basic principles for reconfiguring pathways and the IPC measures that can be adjusted for local needs. Second, certain items such as double swab test before surgery that could be beneficial from an IPC point of view did not reach consensus. This was due to concerns of local resources of the participants and we have proposed several different alternative pathways as shown in Fig. 3. Thirdly, we did not present with a local audit tool for the proposed reconfigured pathways, yet measuring the impact can be useful. However, this was found to be challenging due to the complexity of the pathway. Finally, we only reviewed the pathway for patients with localised prostate cancer that opt for radical surgical treatment. Despite that this cohort can benefit from the

present work, there is more to be done for reconfiguring the pathways for localised prostate cancer.

Future research related to this work should encompass the measurement of the impact of pathway reconfiguration. Such research should prioritise patient-related outcomes including cancer progression, side-effects related to ADT, and functional outcomes following delayed surgery. Furthermore, studies of COVID-19 cold sites should measure the frequency, characteristics, and implications of COVID-19 cases following surgery. The impact on healthcare workforce should also be measured, including their well-being and frequency of hospital-acquired COVID-19. Health economic assessment of the COVID-19 cold sites could be challenging. Nevertheless, the cost and utility of a COVID-19 cold site can be estimated against the absence of such a site during the pandemic.

In summary, the panel reached consensus on two main domains. Firstly, if COVID-19 remains in the community, surgical procedures for the treatment of prostate cancer should be carried out in a setting where the likelihood of COVID-19-related hazards and consequences are kept low. To achieve this, the panel agreed on the concepts to which the healthcare environment, patients, and healthcare workforce must adhere. Secondly, agreement was reached on reconfiguring the management pathways for patients with prostate cancer if significant delay (>3–6 months) in curative management was unavoidable. The EAU risk-classification system was adopted, and the follow-up pathway for each risk group was refined. Finally, some of the broader concepts could be adapted to other indications beyond prostate cancer surgery.

Funding

No funding was received for this project.

Conflicts of Interest

Zafer Tandogdu declares no conflicts of interest.

References

1 **Naspro R, Da Pozzo LF**. Urology in the time of corona. *Nat Rev Urol* 2020; 17: 251–3

2 **Campi R, Amparore D, Capitanio U et al.** Assessing the burden of nondeferrable major uro-oncologic surgery to guide prioritisation strategies during the COVID-19 pandemic: insights from three Italian high-volume referral centres. *Eur Urol* 2020; 78: 11–5

3 **Global Burden of Disease Cancer Collaboration**. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: a systematic analysis for the global burden of disease study. *JAMA Oncol* 2019; 5: 1749–68

4 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Prostate Cancer. Version 4., 2018. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx. Accessed November 2020.

5 **Mottet N, Cornford P, van den Bergh RC, et al**. EAU guidelines: prostate cancer, 2020. Available at: https://uroweb.org/guideline/prostate-cancer/. Accessed November 2020.

6 **Moher D, Liberati A, Tetzlaff J, Altman DG, The PG**. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; 6: e1000097

7 **Iqbal S, Pipon-Young L**. The Delphi method. *Psychologist* 2009; 22: 598–601

8 **Maclennan SJ, Maclennan SJ, Imamura M et al.** Urological cancer care pathways: development and use in the context of systematic reviews and clinical practice guidelines. *World J Urol* 2011; 29: 291–301

9 **Wolfel R, Corman VM, Guggemos W et al.** Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020; 581: 465–9

10 **Wang D, Hu B, Hu C et al.** Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323: 1061–9

11 **World Health Organization (WHO)**. *Rational Use of Personal Protective Equipment (PPE) for Coronavirus Disease (COVID-19), 2020*. Available at: https://www.who.int/publications/i/item/rational-use-of-personal-protective-equipment-(ppe)-for-coronavirus-disease-(covid-19). Accessed November 2020.

12 **Park J, Yoo SY, Ko JH et al.** Infection prevention measures for surgical procedures during a middle east respiratory syndrome outbreak in a tertiary care hospital in South Korea. *Sci Rep* 2020; 10: 325

13 **Lauer SA, Grantz KH, Bi Q et al.** The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med* 2020; 172: 577–82

14 **National Institute of Clinical Excellence (NICE)**. *Reducing the Risk of Transmission of COVID-19 in the Hospital Setting, 2020*. Available at: https://www.nice.org.uk/covid-19/specialty-guide. Accessed November 2020.

15 **Wang CJ, Ng CY, Brook RH**. Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing. *JAMA* 2020; 323: 1341–2

16 **World Health Organization (WHO), Global Observatory for eHealth series**. *Telemedicine: Opportunities and Developments in Member States: Report on the Second Global Survey on eHealth, 2010*. Available at: https://www.who.int/goe/publications/goe_telemedicine_2010.pdf. Accessed November 2020.

17 **Huang Z, Zhao S, Li Z et al.** The battle against coronavirus disease 2019 (COVID-19): emergency management and infection control in a radiology department. *J Am Coll Radiol* 2020; 17: 710–6

18 **World Health Organization (WHO)**. *Coronavirus Disease 2019 (COVID-19) Situation Report – 28, 2020*. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200217-sitrep-28-covid-19.pdf?sfvrsn=a19cf2ad_2. Accessed November 2020.

19 **Lei S, Jiang F, Su W et al.** Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine* 2020; 21: 100331

20 **Wilt TJ, Jones KM, Barry MJ et al.** Follow-up of prostatectomy versus observation for early prostate cancer. *N Engl J Med* 2017; 377: 132–42

21 **Bryant RJ, Oxley J, Young GJ et al.** The ProtecT trial: analysis of the patient cohort, baseline risk stratification and disease progression. *BJU Int* 2020; 125: 506–14

22 **Klotz L, Vesprini D, Sethukavalan P et al.** Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. *J Clin Oncol* 2015; 33: 272–7

23 **Ahmed HU, El-Shater Bosaily A, Brown LC et al.** Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* 2017; 389: 815–22

24 **Shaw GL, Thomas BC, Dawson SN et al.** Identification of pathologically insignificant prostate cancer is not accurate in unscreened men. *Br J Cancer* 2014; 110: 2405–11

25 **Fang D**, **Zhou L**. Androgen deprivation therapy in nonmetastatic prostate cancer patients: Indications, treatment effects, and new predictive biomarkers. *Asia Pac J Clin Oncol* 2019; 15: 108–20

26 **Prem K**, **Liu Y**, **Russell TW et al.** The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. *Lancet Public Health* 2020; 5: e261–70

27 **James ND**, **Spears MR**, **Clarke NW et al.** Failure-free survival and radiotherapy in patients with newly diagnosed nonmetastatic prostate cancer: data from patients in the control arm of the STAMPEDE trial. *JAMA Oncol* 2016; 2: 348–57

28 **Ng HS**, **Koczwara B**, **Roder D**, **Vitry A**. Development of comorbidities in men with prostate cancer treated with androgen deprivation therapy: an Australian population-based cohort study. *Prostate Cancer Prostatic Dis* 2018; 21: 403–10

29 **Ribal MJ**, **Cornford P**, **Briganti A**. EAU Guidelines Office Rapid Reaction Group: an organisation-wide collaborative effort to adapt the EAU guidelines recommendations to the COVID-19 era. *Eur Urol* 2020; 78: 21–8

30 **Teoh JY**, **Ong WL**, **Gonzalez-Padilla D et al.** A global survey on the impact of COVID-19 on urological services. *Eur Urol* 2000; 78: 265–75

Correspondence: Zafer Tandogdu, Department of Urology, University College London Hospital, Westmoreland Street, London, UK.

e-mail: drzafer@gmail.com

Abbreviations: (e)PLND, (extended) pelvic lymph node dissection; (EB)RT, external beam radiotherapy; ADT, androgen-deprivation therapy; AS, active surveillance; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; EAU, European Association of Urology; ECDC, European Centre for Disease Prevention and Control; IPC, infection prevention and control; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Clinical Excellence; PPE, personal protective equipment; RP, radical prostatectomy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Evidence synthesis.
Appendix S2. Prostate cancer international guidelines risk stratification and relevant treatment for non-metastatic prostate cancer.
Appendix S3. International expert panel members.
Appendix S4. Presentations to inform the consensus panel.
Appendix S5. Survey questions and level of consensus on each item.
Appendix S6. Detailed consensus statements.
Appendix S7. Strategies on implementing pre-surgical isolation to decrease the risk of COVID-19 contagiousness risk.